

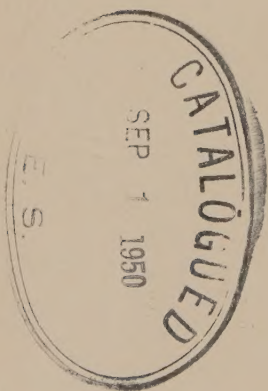
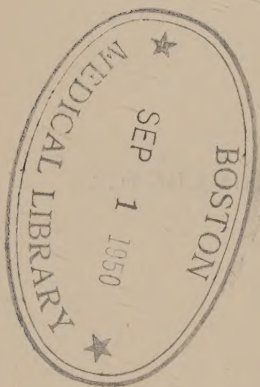
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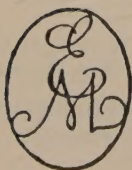
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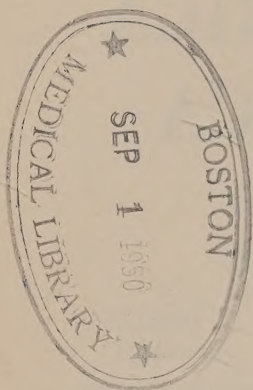
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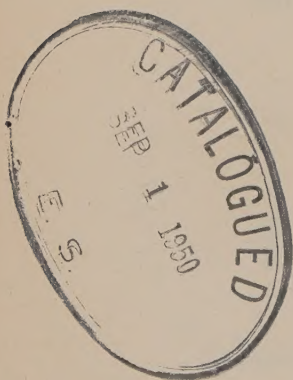


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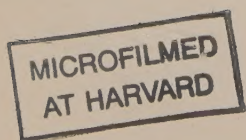


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AN ELECTROENCEPHALOGRAPHICALLY
LOCALIZED FOCUS IN A CASE OF
STURGE-WEBER SYNDROME,
EXTIRPATED WITH GOOD RESULT

BY

BENDT BROAGER and HELGE HERTZ

The combination of unilateral facial naevi with cortical calcifications, and unilateral or bilateral convulsions is well-known under the name of the Sturge-Weber syndrome. As pointed out by *Krabbe* the abnormality not only is a vascular one, comparable to the naevi in the skin or the retina, but is combined with diffuse atrophy of one hemisphere or sometimes involving both.

In these cases, the calcifications seen on the X-ray in the occipital region are not, as was previously considered, abnormal vessels, but deposits of lime in the atrophic cortex. The atrophy usually covers a much larger area of the cortex than suggested by the calcifications seen on the X-rays (*Krabbe* 1934). Air studies of these patients (*Olivecrona* 1936) show a diffuse unilateral ventricular dilatation, corresponding to the diffuse atrophy. Carotid angiography usually is normal (*Olivecrona* 1936) but may show abnormal vessels (*Moniz* 1940), but the atrophy has a far greater extent than the area covered by the abnormal vessels. These facts are important from the point of view of surgical treatment of the epilepsy, which starts in early childhood and is difficult to control by usual medication. The convulsions often are unilateral, but as a rule show no other localizing features; consequently the surgeon has little indication as to which part of the cortex to

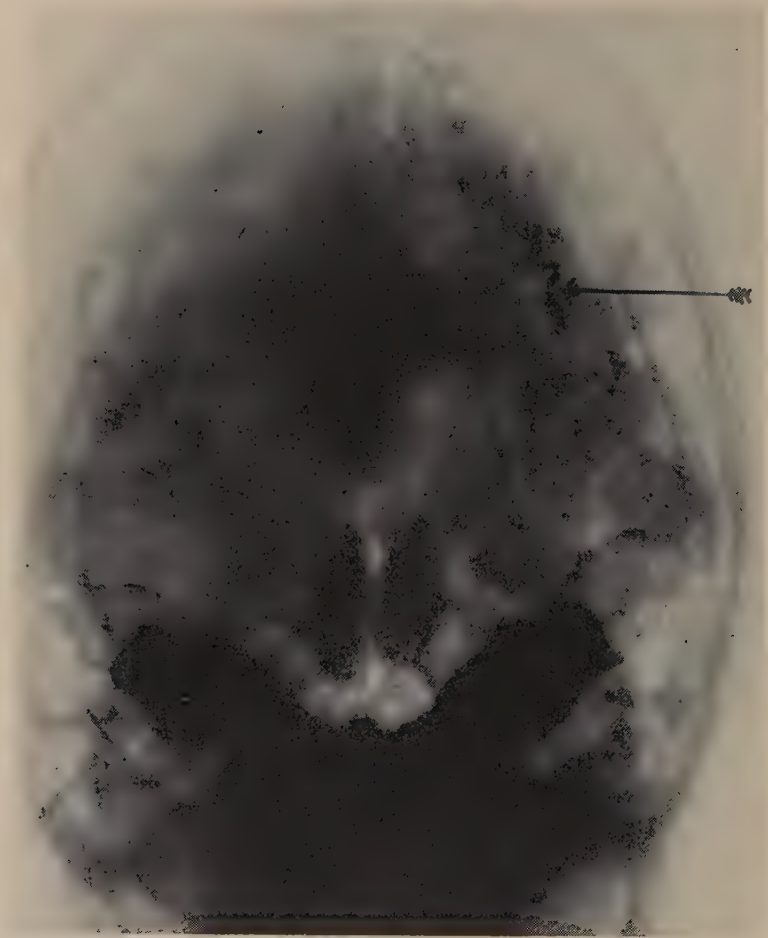


Fig. 1.

Air encephalogram, *Towne's* projection. In the left occipital region the long tortuous calcifications are recognizable.

extirpate. In some cases the occipital cortex corresponding to the conventional site of the calcifications has been removed, but since the atrophy is more extensive, this is no entirely rational procedure, and varying results have been obtained. In the case to be described the localizations of the calcifications and of the epileptogenous focus did not correspond.

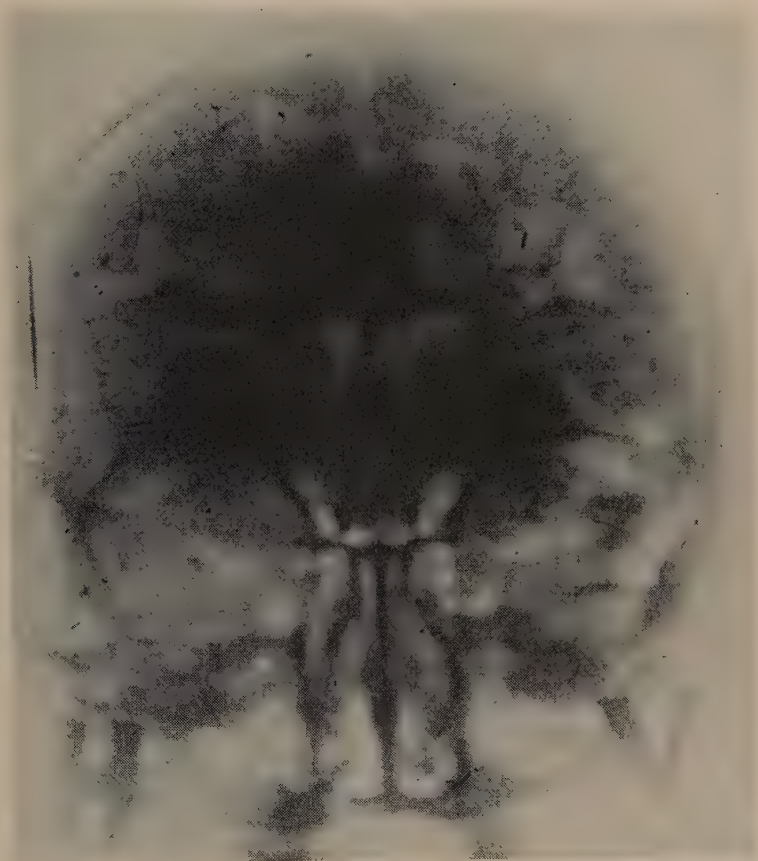


Fig. 2.

Air encephalogram, frontal view. Distribution of air on surface of cortex indicates diffuse atrophy, especially on the left side. Ventricles inadequately filled, slightly dilated.

About one year ago this typical case of the Sturge-Weber-Krabbe disease was treated surgically in the Copenhagen Neurosurgical Clinic, directed only by means of an electroencephalographically localized focus, and it appears that electroencephalography is as yet the only method which gives any indication in these cases.

A summary of the case-history:

The patient was a 5 year old girl, admission 3/3-47, only child, no epilepsy or other diseases in the family. Delivery normal. Since birth a naevus flammeus, covering the left forehead, the left periorbital region, left side of nose, and extending over the upper lip. Since she was one year old she had

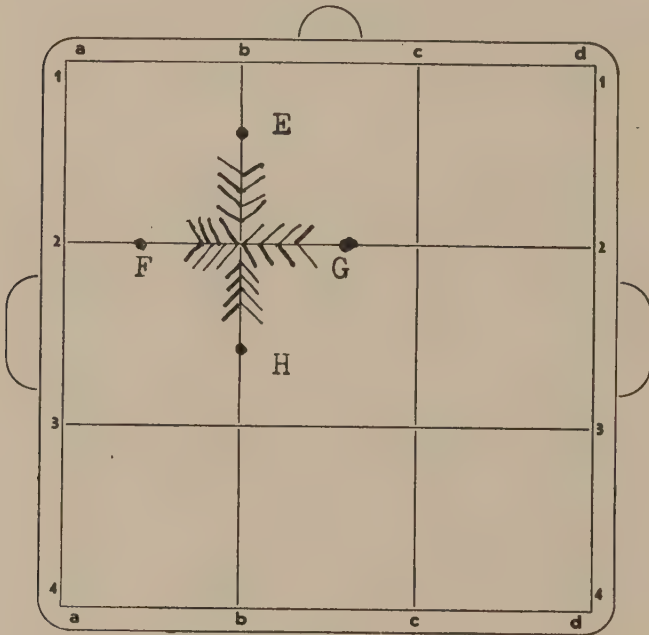


Fig. 3.

Diagram of electrode arrangement. The electrodes are indicated 1 a, 1 b, etc. The constant phase reversal indicated at 2 b. E, F, G, and H are the extra electrodes applied to secure localization at 2 b.

convulsions, always starting in the right arm or leg, followed by temporary right-sided hemiparesis. Mental progress had been rather slow. In spite of medication with luminal 45 mg. + 45 mg. + 60 mg. daily, the severity and frequency of the convulsions increased, and the patient continued to have epileptic attacks ten times per day.

On admission the child was restless, the naevus flammeus

as described. In the left half of the left retina there was increased vascularity and the vessels were tortuous; there was a right-sided paresis of the sixth nerve, but no other abnormal neurological signs. X-rays of skull (Fig. 1) showed the typical tortuous calcifications in the left occipital region. Suboccipital encephalography (Figg. 1-2) showed slight diffuse dilatation of the ventricular system, more marked on the left than the right, and abnormal distribution of air over the left hemisphere, typical of atrophy. Cerebrospinal fluid normal. WR. negative.

Electroencephalography (Fig. 4 a) showed diffuse, almost continuous spike and wave formation over the whole cortex, but with bipolar leads there was a left-sided parasagittal premotor focus with constant phase reversals. The point was marked with mercurochrome on the scalp, and recordings on three successive days gave identical results. The position of the focus was further defined by applying extra electrodes midway between the electrodes (Fig. 3) normally used for bipolar leads. The electroencephalogram showed other less pronounced phase reversals, which, however, were not constantly present in the different sessions.

On operation (*Broager*) a left-sided Dandy incision was made extending across the midline, and exposing the whole of the left premotor region. The dura appeared normal on the surface, but on the inside it was found to be covered by a large naevus, which extended backwards over the motor region. There were small adhesions between the dura and the cortex, but no large vessels. The arachnoid membrane was diffusely milky with collections of fluid underneath, and with a net of adhesions to the cortex, especially in the parasagittal region. The cortex showed slight microgyri, and a number of fine tortuous pial vessels. The alterations were diffuse, as in the pathological specimens described by *Krabbe*.

At this stage it was attempted to provoke convulsions from the point of the parasagittal focus by stimulation with a square wave generator and two pointed platinum electrodes (*Penfield* 1941). Probably due to the general anæsthesia (100 mg. avertin per kilo and chloral hydrate) this was, however, not suc-

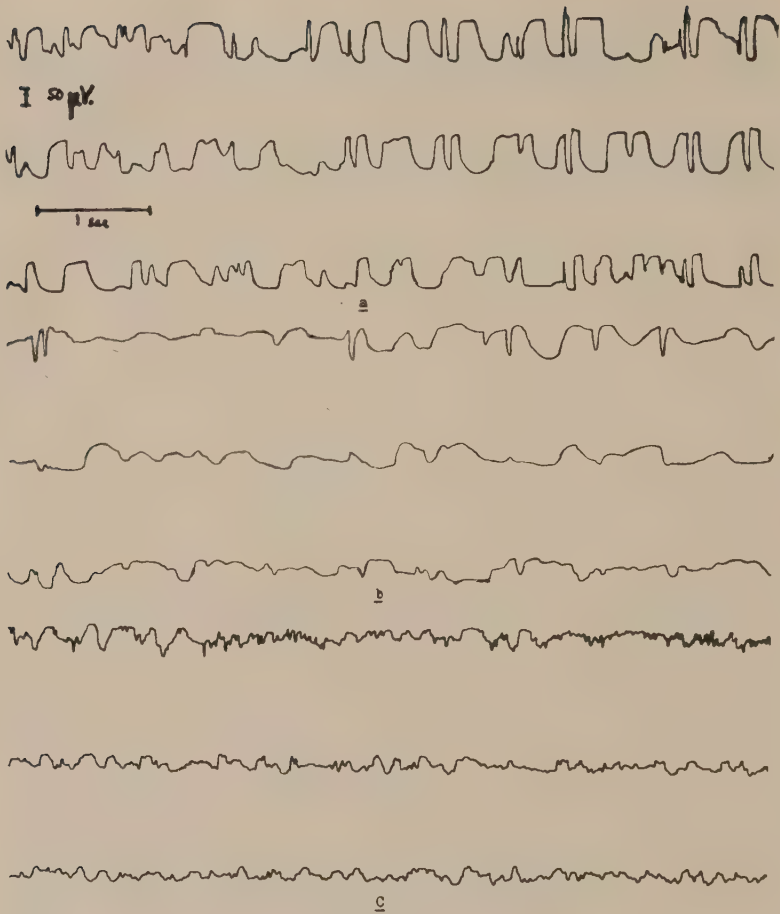


Fig. 4.

Electroencephalograms. a, before operation, b, one week after operation, c, one year after operation. The three electroencephalograms are taken in the lead: longitudinal b. (cf. Fig. 3). At part a the phase reversals between the two upper leads are clearly indicated. Otherwise all leads had the same appearance. c still shows some dysrhythmia.

NB. the patient is six years of age.

cessful. The child was too restless for operation under local anaesthesia.

An "en bloc" resection of the whole parasagittal premotor

region was performed, the naevus on the inside of the dura was coagulated, the dura closed and the craniotomy finished in the usual way.

In the first week after operation there was a right-sided hemiparesis, which subsided completely, and recovery was otherwise uneventful. An electroencephalogram one week after operation showed diffuse slow waves over the whole cortex, but without spike and wave formations or phase reversals (Fig. 4 b).

One year after operation the patient was completely changed, calm; on luminal 50 mg. + 50 mg. + phenantoine 100 mg. she had had no epileptic seizures since operation, but she still had some attacks of "petit mal", usually occurring at a three weeks' interval, two or three attacks during a period of two days. On examination she had no signs of neurological abnormalities other than those present at the first examination. Electroencephalography showed some 4-7 cycle waves, but was without spike and wave formations or phase reversals (Fig. 4 C).

This case is of interest from several points of view:

- (1) The focus which was removed at operation was localized only by means of the electroencephalogram, in the absence of any other criterion, and the later course indicates that it was the epileptogenous focus of the patient.
- (2) Although the patient had had attacks for four years at the time of operation, and had diffuse pathological and electroencephalographic alterations, a considerable improvement of the condition, or perhaps a cure, could still be achieved by the removal of a well localized focus. In this respect the case deviates from the cases of posttraumatic epilepsy described by *Dennis Williams* (1944), where it was stated that a focus, which was not removed, was quickly generalized.

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KLINISCHE ERFAHRUNGEN
AN GEISTESKRANKEN
MIT LYSERGSÄURE-DIÄTHYLAMID

VON
GION CONDRAU

Die pharmakologische Analyse der Mutterkornalkaloide brachte der medizinischen Erkenntnis vegetativer Störungen in diagnostischer und therapeutischer Hinsicht wertvolle Grundlagen. Im Jahre 1943 wurden im Mutterkornlaboratorium der Sandoz A.-G. in Basel durch Dr. phil. A. Hofmann erstmals bei einem Abkömmling des Mutterkorns eigentümliche psychische Wirkungen festgestellt; sie wurden 1947 von W. A. Stoll' an unserer Klinik näher beschrieben. Es handelt sich um das Lysergsäure-diäthylamid (LSD), einen Stoff, „der in ungeahnt geringen Dosen das seelische Geschehen wiederholbar gleichsinnig“ beeinflusst.

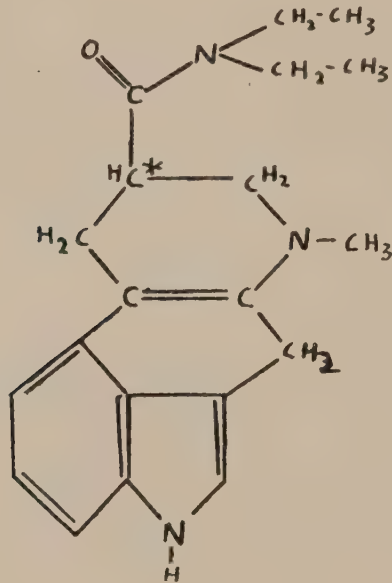
PHARMAKOLOGISCHES

LSD ist das künstlich hergestellte Amid der allen Mutterkornalkaloiden zugrunde liegenden d-Lysergsäure mit einem sekundären Amin, dem Diäthylamin, und stellt somit einen (partialsynthetischen) Vertreter der Ergobasingruppe dar.

Das LSD besitzt wahrscheinlich folgende chemische Formel:

Da das LSD schwer wasserlöslich ist, wird es in Form des leicht löslichen Tartrats verwendet. Bei pharmakologischen Versuchen wurden an narkotisierten Tieren nach der Injektion von LSD neben einer gewissen Uteruswirksamkeit Auf-

regungszustände und anderseits „eigentümliche Zustände motorischer Starre, bei denen man an katatonie Bilder zu denken geneigt war“ festgestellt (Stoll¹).



BISHERIGE VERSUCHSERGEBNISSE

Stoll¹ verabreichte das LSD 29mal 16 Normalpersonen und 20mal 6 schizophrenen Patienten. Er gelangte zu dem Ergebnis, das LSD erzeuge einen Rauschzustand im Sinne des akuten exogenen Reaktionstypus. Neben motorischen und vegetativen Symptomen traten, zumal bei seinen Versuchen an Geistesgesunden, Störungen der Wahrnehmung, vor allem optische Halluzinationen auf, die mit einer leichten Bewusstseinsstrübung bei teilweise erhaltener Selbstbeurteilung einhergingen. (Auf Grund dieser auffälligen optischen Wahrnehmungsstörungen stellt das LSD ein Eidetikum im Sinne *Hellpach*'s² dar, während es allgemein als Phantasticum bezeichnet werden kann.) Der Gedankengang war bei starker Ablenkbarkeit meist beschleunigt, die Stimmung schwankte vorwiegend nach der

euphorischen, aber auch nach der depressiven Seite hin. Als Nachwirkungen des LSD-Rausches traten u. a. mnestiche Störungen auf. Stoll vertritt die Ansicht, der LSD-Rausch sei weitgehend unspezifisch, wie dies wahrscheinlich auch bei den durch andere Rauschgifte erzeugten Zustandbildern der Fall sei. Eine dem LSD jedoch bisher allein zukommende und theoretisch bedeutsame Eigenschaft ist dessen Wirksamkeit in der minimalen Menge von 20 bis 30 gamma ($0,00002$ — $0,00003$ g). Es handelt sich also um einen hochwirksamen Spurenstoff, dessen Wirksamkeit sich in so kleinen Dimensionen bewegt, dass sich die Frage aufdrängt, ob nicht bei spontanen Psychosen, deren endotoxische Natur seit langem vermutet, aber nie erwiesen werden konnte, ähnliche Giftstoffe eine Rolle spielen könnten.

FRAGESTELLUNG, AUSGANGSMATERIAL, METHODIK

Die Versuche Stoll's an geistesgesunden und psychotischen Versuchspersonen warfen die Frage nach der therapeutischen Wirkung und einer eventuellen diagnostischen Verwertbarkeit des LSD auf. Die überaus starke psychische Wirksamkeit des LSD liess den Versuch lohnend erscheinen, dessen Verwendbarkeit in der psychiatrischen Diagnostik und Therapie an einem grösseren klinischen Material zu überprüfen. Weiter erscheint die Frage bedeutungsvoll: Verhält sich der Stoffwechsel bezüglich dieses Mutterkornabkömmlings bei Psychosen anders als bei Geistesgesunden? Spielen vielleicht im Stoffwechsel von Geisteskranken ähnliche Stoffe wie das LSD eine Rolle?

Es erschien deshalb auch uns wichtig, die Wirkung dieses Phantasticums bei Normalpersonen und Geisteskranken zu vergleichen. Wir stellten uns die Frage: Zeigen sich hinsichtlich des Zeitpunktes des Eintretens der Wirkung bei Gesunden und Geisteskranken Unterschiede? Betreffen solche die Wirkungsdauer? — Dürfen hinsichtlich der Dosierung, der Regelmässigkeit und Art der Wirkung Unterschiede erwartet werden? — Wir stellten uns weiter die Frage nach der Brauch-

barkeit des LSD als vorübergehend euphorisierendes Mittel oder im Sinne der Schocktherapie.

An der psychiatrischen Klinik der Universität Zürich habe ich nach den Versuchen *Stoll's* insgesamt 197 LSD-Versuche bei 30 geisteskranken Probanden durchgeführt, dazu 7 Versuche an normalen Versuchspersonen (Assistenzärzte der Klinik und ein Selbstversuch des Verfassers), die als Kontrollversuche bewertet werden müssen. Im allgemeinen wurden die gleichen Versuchsbedingungen eingehalten, wie sie *Stoll* in seiner Arbeit beschrieben hat. Für die Durchführung der LSD-Kuren wurde prinzipiell, wie bei jeder Schockbehandlung in unserer Klinik, die Einwilligung der Angehörigen eingeholt; die Patienten wurden, soweit dies möglich war, über das Mittel aufgeklärt. Weigerte sich eine Versuchsperson aus irgend einem Grunde, das Mittel zu nehmen, so wurde auf die weitere Durchführung der Kur verzichtet.

Die Auswahl der Kranken erfolgte nicht nach einheitlichen Gesichtspunkten hinsichtlich der Diagnose. Im Allgemeinen wurden Patienten herangezogen, bei denen die übliche Therapie mit Schockkuren versagt hatte oder aus irgend einem Grunde nicht durchgeführt werden konnte. Auch trachteten wir danach, für die Durchführung der Versuche Probanden zu gewinnen, die einigermaßen differenziert und willig waren, über ihre seelischen Erlebnisse Auskunft zu geben. — Die Dosierung des Mittels sowie die Anzahl der Versuche wurden gewöhnlich dem jeweiligen körperlichen und geistigen Zustand des Patienten oder dessen besonderem Krankheitsbild angepasst und je nach den gemachten Erfahrungen weitergeführt oder abgeändert.

Praktisch wurden die Versuche so durchgeführt, dass einer Gruppe von 2 bis 7 Versuchspersonen morgens ca. um 08.00 U. das LSD (1:50'000) in Form einer wässrigen Lösung peroral, anfänglich nüchtern, später im Anschluss an das Frühstück, verabreicht wurde. Teilweise wurden die Versuchspersonen den ganzen Vormittag im Bett gehalten, meistens jedoch liessen wir sie aufstehen und besammelten sie unter der Kontrolle des Pflegepersonals und eines Arztes in einem geeigneten Arbeitsraum. Es wurde ihnen eine leichte Beschäftigung zugewiesen oder sie wurden angehalten, in Zeitschriften oder Büchern zu lesen. Während des Vormittags wurden ausführliche Protokolle über das körperliche und psychische Befinden der Versuchspersonen geführt. Stündlich wurden Blutdruck und Puls gemessen, auf der Höhe der LSD-Wirkung wurde eine neurologische Untersuchung durchgeführt. In regelmässigen Abständen wurden Laboratoriumsuntersuchungen (Blutbild und Urinuntersuchungen) vorgenommen. Hinsichtlich des psychischen Verhaltens wurde vor allem auf die Grundstimmung und eventuelle Veränderungen derselben geachtet, ferner auf die Bewusstseinslage, den Gedankengang, sowie auf wahnhafte Einstellungen und Sinnestäuschungen, insbesondere Illusionen

und optische Halluzinationen. — Bei besonders eindrücklichen Zustandsbildern wurden die Versuchspersonen in ein verdunkeltes Zimmer geführt, um das Vorhandensein und die Intensität der Sinnestäuschungen besser feststellen zu können.

Im allgemeinen begannen wir mit einer niederen Dosierung von 20—40 gamma und steigerten in den folgenden Tagen die Dosis, bis wir aus äusseren Gründen oder wegen körperlicher oder psychischer Unverträglichkeit des Mittels die Kur abbrechen mussten. Wir trachteten darnach, eine lückenlose Kur von 6—10 Tagen durchführen zu können, schalteten jedoch auch Versuche ein, bei denen wir nur jeden 2. Tag das Mittel verabreichten. Andere Male wiederum zwangen uns verschiedene unvorhergesehene Gründe (Auftreten einer körperlichen Erkrankung, allzustarke psychische Erregtheit des Patienten usw.) die Kur vorübergehend abzubrechen und erst nach einiger Zeit wieder weiterzuführen. In einigen Fällen variierten wir die Dosierung insofern, als wir nach Tagen höherer Dosierung wiederum kleinere Dosen verabreichten, in Anlehnung an die sogenannte Schaukelmethode bei der Insulinkur. In 4 Fällen wurde das Mittel nur einmal verabreicht; bei den übrigen Versuchspersonen 2 bis 16 mal. In 19 Fällen betrug die Höchstdosis des LSD 100 gamma und mehr. Die höchste Dosierung wurde bei einer 16-tägigen Kurdauer mit 280 gamma erreicht.

Wir verzichteten im allgemeinen darauf, die Vielfalt der psychischen Symptome durch die Anwendung vieler Tests in ein starres und einseitiges Schema zu zwingen. Es handelte sich vor allem um eine klinische Beobachtung, wie sie auch bei den übrigen Geisteskranken der Klinik durchgeführt wird. — Nachmittags wurden die Versuchspersonen wieder auf ihre Abteilungen versetzt, wo sie weiterhin unter Kontrolle und Beobachtung standen.

Wir können gleich vorwegnehmen, dass sämtliche Versuche ohne ernsthafte oder gar bedrohliche Zwischenfälle verliefen.

KONTROLLVERSUCHE AN NORMALPERSONEN

U. a. machte *K. Zucker*³ im Jahre 1932 auf den Wert der Rauschgiftselbstversuche aufmerksam. Besonders hinsichtlich des Verhältnisses der Persönlichkeit zu den psychischen Erscheinungen während einer Vergiftung sollen solche Versuche aufschlussreich sein.

„Wie jemand zu denken, zu erleben gewohnt ist, d. h. auf Grund seiner ihn zu einer bestimmten Denkform erziehenden Umgebung, also mit wie gearteten Vorstellungs- oder Erlebensmöglichkeiten er bislang zugebracht hat, das wird auch den Inhalt seiner Erlebnisse im Rausch-

zustand mitbedingt gestalten.“ Rauschgiftversuche haben „darüber hinaus und unabhängig von Standpunktsverschiedenheiten einen ganz andern Wert. Dieser ist in erster Linie an den Selbstversuch geknüpft. Ist es überhaupt schon für den Psychiater eine Bereicherung, mal sozusagen eine Psychose an sich selbst erlebt zu haben, so liegt die Hauptbedeutung eben in der Möglichkeit, die Entwicklung mancherlei psychotischer Erscheinungen selbsterlebend verfolgen zu können. Natürlich ist im einzelnen diese Möglichkeit auch wieder bis zu einem gewissen Grade abhängig von Fähigkeit, Gewöhnung und Neigung zur Selbstbeobachtung.“

Die an Geistesgesunden und ebenfalls unter spezieller psychiatrischer Kontrolle und Selbstkontrolle durchgeführten Versuche bestätigten die *Stoll'schen* Ergebnisse, wobei in den Eigenberichten oft wörtlich identische Formulierungen vorlagen. Sie sollen hier kurz zusammengefasst werden: Motorische Störungen (Ataxie, positiver Romberg, breitspuriger Gang, undeutliche Sprache, Veränderung der Schrift); gröbere neurologische Symptome traten nicht auf, hingegen in einigen Fällen Steigerung der Sehnenreflexe; vegetative Symptome (Schwindelgefühl, Herzklopfen, Unwohlsein, Erbrechen, schlechte oder stark gerötete Gesichtsfarbe, Akrozyanose, Wadenkrämpfe, Hitze- und Kältegefühl, Hypersalivation); Störungen der optischen und akustischen Wahrnehmung (starkes Farberleben, wobei besonders die rote Farbe an Intensität gewann, illusionistische Umdeutung von Geräuschen); Störungen des Geschmacks (Fadheit der Zigarette, Metallgeschmack im Munde). Eine eigentliche Störung der Bewusstseinslage wurde, abgesehen von einem „Kater-“ oder „Rauschgefühl“ nicht beobachtet. Es zeigte sich auch bei unsern Versuchen, dass die Fähigkeit zur Selbstbeurteilung nie aufgehoben war; jede Handlung wurde trotz der Enthemmtheit registriert und bewertet. Der Gedankengang erwies sich als gelockert und beschleunigt und stark ablenkbar, wobei weniger die Ideenflucht als eine gewisse Perseveration, d. h. ein immer wiederkehrendes Zurückgreifen auf ein verlassenes Thema auffiel. Die Stimmung veränderte sich im Sinne einer Verstärkung und besonders deutlichen Akzentuierung der vorbestehenden Grundstimmung. — Die durchgeführten Versuche zur Bestimmung der Konzentrationsfähigkeit (Kräpelin'scher Rechen-

versuch, Test de Bourdon und Stokvisde Wind'scher Rechen-test) ergaben eine merkliche Verminderung derselben gegenüber dem normalen Verhalten. Die Schwankungen blieben jedoch im Bereiche der Norm.

In einem Falle wurden bereits mit 20 *gamma* LSD deutliche Veränderungen wahrgenommen. Vor allem zeigten sich vegetative Störungen wie leichtes Schwindelgefühl, Gefühl der Leere im Kopf, Hypersalivation. Obschon das Mittel an sich geruchlos ist, hinterliess es eigentümliche Geschmackssensationen im Sinne eines faden, metallenen Geschmacks, der immer stärker wurde und, abgesehen von der Essenszeit, den ganzen Tag anhielt.

Eigentliche motorische Störungen wurden bei dieser Dosierung nicht bemerkt, ebenso fehlten Störungen der optischen oder akustischen Wahrnehmung. Die Stimmung war eher euphorisch und zeitweise, besonders in der ersten Zeit der LSD-Wirkung trat ein als Zwangslachen empfundenes „dauerndes unmotivierbares Schmunzeln“ auf, das sich bis zum Lachkrampf steigern konnte. Ebenso auffällig waren die psychischen Erscheinungen: plötzliches Nachlassen des Arbeitseifers, ein Zustand innerer Unrast und Unruhe, subjektiv empfundene Konzentrationsschwäche. Einem selbstverfassten Protokoll entnehmen wir in Kürze:

(Prot. 1, Arzt, 20 *gamma* LSD).

„Der Arbeitseifer liess plötzlich nach, ich lief die ganze Zeit im Büro umher, ohne auch nur das geringste zu tun. Ich wäre nicht einmal fähig gewesen, einen Brief zu schreiben. Trotzdem befand ich mich in einem innerlichen sehr tätigen Zustand: das Wissen um mein „Nichtstun“ beschwerte mich nicht im geringsten. Ich fand es als selbstverständlich.“ Dazu kam eine beinahe paranoide Einstellung zur Umwelt, die allerdings reaktiv bedingt sein mochte. „Ich glaubte jedermann sehe mich besonders scharf an, beobachtete mich und müsse mich irgendwie verändert finden. Ich schämte mich, Dr. St. zu begegnen und hatte das Gefühl, ganz rot zu werden, wenn mich jemand anschaute. Auch fand ich es höchst einfältig, dass ich ständig lachen musste.“ Dazu kam ein subjektives Empfinden von Schwere in den Gliedern, ebenso ataktische Störungen. „Ich hatte das Gefühl, wenn mich jemand berühren oder leicht stossen würde, würde ich umfallen. Beim Rombergversuch hatte ich subjektiv das Gefühl zu

schwanken, obwohl dies nicht der Fall war.“ Ein eigentliches Silbenstolpern wurde nicht bemerkt, jedoch andeutungsweise erschwertes Sprechen. „Die Zunge war zeitweise etwas klobig, ich wäre kaum fähig gewesen, beispielsweise eine längere Rede zu halten.“ Die Schrift war nicht verändert, hingegen bestand subjektiv ein leichtes Gefühl des Unsicherseins beim Schreiben, wobei gelegentlich auch Buchstabensperrungen auftraten. Es bestand ferner ein starkes Mitteilungsbedürfnis, zeitweise direkt ein Rededrang. „Während des Konzentrationsversuches hatte ich jedoch das Gefühl einer deutlichen Konzentrationsschwäche. So gingen mir allerhand Gedanken durch den Kopf, die ich einfach nicht verbannen konnte.“ Während des Nachmittages verflüchtigten sich sämtliche Erscheinungen, dagegen trat gegen Abend ein leichtes Krankheitsgefühl auf, ähnlich wie in der „Rekonvaleszenz einer leichten fieberhaften Erkrankung“.

Zwei Versuche mit je 30 *gamma* LSD machten keine Erscheinungen, während bei 40 *gamma* sehr deutliche Symptome auftraten. Zwei Versuchspersonen wurde — nachdem sich dieselben prinzipiell damit einverstanden erklärt hatten — an einem nicht genau bestimmten Tage unbemerkt je 40 *gamma* LSD beim Morgenkaffee gegeben, um jeglichen auto-suggestiven Einflüssen vorzubeugen. Die folgenden Protokollauszüge sind hinsichtlich der psychiatrischen Symptomatik sehr aufschlussreich:

(Prot. 2, Arzt, 40 *gamma* LSD).

„Ca. um 10 Uhr Auftreten eines allgemeinen Hitzegefühles, das sich langsam steigerte bis es zu deutlichem Schweissausbruch kam, der auch von der Umgebung wahrgenommen wurde. Gleichzeitig stellte sich eine zunehmende Konzentrationsschwäche ein. Ich brauchte ungefähr eine Viertelstunde bis ich zwei Telephonnummern im Verzeichnis gesucht und gefunden hatte. Das Interesse an der Büroarbeit schwand vollkommen. Ich konstatierte eine zunehmende motorische Erregung, die sich in einem Beschäftigungsdrang äusserte und mich zwang, andauernd im Büro umherzugehen, wobei ich Gegenstände und Akten auf dem Tisch verschob, hier und dort in einer Krankengeschichte blätterte, ohne mich aber nur im geringsten konzentrieren zu können. Dieser Zustand war mit dem subjektiven Gefühl einer starken Euphorie verbunden und erschien mir ganz natürlich. Ich fühlte mich leicht, fast schwebend, dachte weder an Vergangenes noch Zukünftiges und realisierte auch nicht, dass ich eventuell vom Phantasticum LSD erhalten haben könnte..... Verglichen mit der mir bekannten Pervitinwirkung erschien mir der Effekt des LSD ein

vielfacher. Es bestand ein eigentlich manisches Bild. Im Zimmer zog ich den Telefonstecker aus, um in diesem schönen Zustand nicht gestört zu werden und legte mich aufs Bett. Der Beschäftigungsdrang zwang mich aber sofort wieder, im Raum herumzugehen, eine angezündete Zigarette liess ich wieder liegen, um in einem Kunstatlas zu blättern, dann ass ich einige Birnen halb und musste dazu immerfort lachen. Ich begann auf die Schreibtischplatte zu trommeln und wurde durch diese Tätigkeit zu weiterem unwiderstehlichem Lachen gereizt..... Es erschien mir nun, als ob alle Anwesenden mich mit grossen, dunklen Augen fortwährend anstarrten. Als mir eine Messingdeckse entgegengestreckt wurde, schreckte ich zurück, weil sie mir plötzlich als lebend erschien. Objektiv wusste ich genau, dass sie nur aus Metall bestand, aber im beschriebenen Moment hatte ich ebenso deutlich das subjektive Gefühl, das Tier bewege sich und öffne seinen Rachen..... Ein frisch gewichster Parkettboden schien mir plötzlich in intensives orange gehüllt..... Auf einmal spürte ich starke Wadenschmerzen und ich hatte das Gefühl, es trete jeden Moment ein Wadenkrampf beider Beine auf. Ich setzte mich auf den Boden und zappelte lachend mit den Beinen..... Im Dunkelmzimmer zeigten sich deutliche optische Halluzinationen elementarer Art. Es bewegten sich unzählige helle Punkte und Fäden wirr durcheinander, die durch ruhende helle Bänder, wie die Strahlen von Flakscheinwerfern, durchkreuzt waren. Ich erstaunte deswegen durchaus nicht, sondern fand diese Erscheinungen normal und betrachtete sie selbstversunken und vergnügt. Der Bulbusdruck verursachte einen beweglichen Wirbel ähnlicher Erscheinungen, die aber, wie auch die vorgenannten, alle farblos, dh. weiss waren. — Gegen 12 Uhr klang der manische Zustand langsam ab und machte einem ganz andern Platz. Daran war am hervorstechendsten eine Kontaktlosigkeit der Umwelt gegenüber. Ich registrierte zwar alles, vermochte mich aber keineswegs in affektive Beziehung dazu zu setzen. Antistisch abgeschlossen schien ich mich wie in einer zähflüssigen Masse darin zu bewegen. Die Denk- und Bewegungsabläufe wurden schwer verlangsamt. Die Impulse zur Bewegung fehlten, ich sprach spontan nichts. Alles bereitete unsäglich Mühe und erzeugte das Gefühl einer allerdings nicht unlustbetonten Hilflosigkeit..... Abends konnte ich kaum einschlafen trotz der starken Müdigkeit, weil ich verschiedene Nachtgeräusche illusionistisch umdeutete und jedesmal aufschreckte.“

(Prot. 3, Aertzin, 40 gamma LSD).

„Ich fühlte mich irgendwie beschwingt und empfand keinerlei Gewissensbisse, dass ich meine Arbeitszeit mit Schwatzen verbummelte... Dann musste ich auch immer mehr lachen über alles und jedes. Es war mir vollkommen gleichgültig, wie ich mich benahm und was ich tat... Immer hatte ich dann auch die merkwürdige Empfindung, dass alle Leute mich anstarrten, und es war auffallend, dass ich bei allen die Pupille

stechnadelartig aus dem Auge hervortreten sah. Mein Gesichtsfeld schien mir röhrenförmig eingeengt, denn ich sah von einer Person nur den Kopf oder die Brust, war aber nicht mehr fähig, die Personen als ganzes zu erfassen. Ich wurde immer mehr zu allerlei Dummheiten aufgelegt, einem Kollegen stülpte ich zB. einen Aschenbecher über den Kopf, ohne mich vorerst zu vergewissern, ob dieser leer oder gefüllt sei. An den Wänden der Korridore sah ich Farbstreifen in grünlichen, orangen und roten Farbtönen. Alles um mich herum sah ich voll grössere und kleinere, unregelmässig begrenzte grau-weiße Flecken auf schwarzem Grund, die sich allmählich in helle dünne Fäden auflösten und Schlingen und Schleifen bildeten. Diese Erscheinungen befanden sich in ständiger Bewegung und wechselten immer wieder ihre Anordnung. Schliesslich schien sich alles an die Peripherie zu bewegen und von dort schob sich alles wieder gegen die Mitte vor und zwar schien es mir, wie wenn diese vielen hellen Bänder in der Mitte in einen Abgrund hineingesaugt würden. Im Zentrum war ein wildes Durcheinander, ein Wirbel oder Strudel, es machte mich ganz schwindlig... Das Essen schmeckte mir gar nicht, ich fand es weder schlecht noch gut und der fade, metallische Geschmack auf der Zunge wurde immer stärker... Gegen Mittag empfand ich alle Farben, besonders aber die orangeroten Töne abnorm intensiv. Oft musste ich meine Augen wegwenden, weil mich die Intensität der Farben direkt schmerzte... Schliesslich bekam ich immer mehr das Gefühl einer starken Isolierung. Ich hatte mit meinen Kollegen keinen rechten Kontakt mehr. Ich versuchte ihnen immer wieder meinen Zustand zu schildern, hatte aber das deutliche Empfinden, dass sie mich nicht verstehen könnten. Es war mir einfach nicht möglich, mich mit ihnen wie sonst in Beziehung zu setzen... Als ich die Augen schloss, traten plötzlich wunderschöne Farbenhalluzinationen auf. Mir war, wie wenn ich unter einem grossartigen Gewölbe stände und in die Höhe blickte. Ich sah dabei wunderbare farbige, mosaikartige Bilder, die phantastische Ornamente bildeten. Die Farbenzusammenstellungen waren oft sehr gewagt, wurden aber immer als schön empfunden. Diese Bilder wechselten kaleidoskopartig und es war mir nicht möglich, die einzelnen näher zu erfassen. Plötzlich sah ich auch etwas völlig anderes, nämlich verschiedene fremdartige, groteske Maskengesichter in phantastischen Farben. Die Masken erschreckten mich jedoch gar nicht, denn sie hatten alle ein freundliches Aussehen und lachten. Ein anderes Mal sah ich auch über ein Dutzend Augen in zehnfacher Vergrösserung wahllos im Raume verteilt. Die Augen waren weit geöffnet, hatten wunderbare Irisfarben und blickten mich wohlwollend an... Am nächsten Tage traten Wadenkrämpfe auf, die mich immer wieder zwangen, die Beine zu schlenkern und zu schütteln. Die Nachwirkungen dauerten beinahe eine Woche. Um überhaupt arbeiten zu können, nahm ich während drei Tagen täglich 1—2 Tabletten Pervitin, was aber merkwürdigerweise keine Wirkung hatte. Normalerweise reagiere ich schon

auf 1 Tablette Pervitin sehr stark. Erst nach einer vollen Woche fühlte ich mich wieder wie vor dem Versuch.“

(Prot. 4, Arzt, 40 gamma LSD).

„Um 1 Uhr beim Klavierspiel: Bedürfnis nach Schnelligkeit, Unsicherheit im Anschlag, Schwierigkeit zu disponieren, vorauszudenken, bei Gedächtnislücken zu improvisieren. Wegfall gewisser Hemmungen, Bedürfnis nach Heftigkeit, Unmöglichkeit aufzuhören. Auf dem Wege nach Hause eigenartiges Gefühl, dass mich alle ansehen, obwohl ich mir Mühe gegeben, so normal als möglich zu erscheinen. Ich glaubte immer wieder, dass die Leute stehen bleiben, um mich anzusehen. Gefühl einer affektiven und geistigen Verarmung. Ich werde mir selbst unerträglich, fühle mich wie in einem Zwangszustand.“

(Prot. 5, Arzt, 40 gamma LSD).

„Empfindung, wie wenn mein Körper leichter als sonst wäre. Beim Heraufgehen der Treppe zum Aertztebüro subjektiv etwas unsicher auf den Beinen, wie bei einem leichten Schwips... ich kann nur mit Mühe ein ganz unbegründetes Lächeln unterdrücken. Im Aertztebüro, wo ich meine Post hole, erscheint mir alles unverändert, aber doch etwas distanziert und fremdartig... Ich muss manche Sätze 3 und 4mal hintereinander lesen, ohne sie deswegen dann zu verstehen. Einigemal setzt das Konzentrationsvermögen bei bewusster Anspannung nochmals für jeweils einige Minuten ein; diese Momente, in denen nahezu volles Verständnis des Gelesenen möglich ist, werden aber immer kürzer. Die Buchstaben fangen an, sich zu verändern, indem gewisse Worte, die mir in irgend einer Hinsicht wichtiger sind als die andern, nun deutlich etwas grösser erscheinen. Der (von einem Philosophen geschriebene) Aufsatz kommt mir schliesslich als leeres Gewäsch vor, obwohl ich daneben ganz deutlich das Bewusstsein habe, dass er es natürlich gar nicht ist. Diese Zwierspältigkeit befremdet mich aber eigentümlicherweise gar nicht, ich lege das Heft weg, sitze etwa eine Minute lang ziemlich antriebslos am Tisch. Beim Aufstehen überrascht mich, dass ich mich körperlich ganz leicht fühle, fast als könnte ich schweben. Eine wohlige Wärme fühle ich vom Rücken aus auf meine ganze Haut ausstrahlen... Auch ganze Sätze, die zusammenfassenden Charakter haben, erscheinen im Druck deutlich um ein Drittel grösser als die andern. Die Buchstaben und Worte sehe ich ganz scharf, nur kommt es mir manchmal bei längerem Hinsehen vor, wie wenn sie sich gleitend leicht bewegten. Ich weiss aber, dass dies natürlich nur meine Einbildung ist. Das Spannungsgefühl im Kopf, in welchem es „wie ein Dröhnen“, aber nur leicht ist und im ganzen Leib hat deutlich zugenommen. Ich habe das Bedürfnis zu tanzen, so leicht fühle ich mich und tue es auch alleine im Zimmer während einigen Minuten. Dann lege ich mich aufs Sofa, denke an nichts, fühle mich

überall angenehm warm. Doch dann fährt mir plötzlich ein kalter Schauer über den Rücken und nun friere ich bald richtig sodass ich rasch aufstehe und mir einen wollenen Pullover anziehe... Beim Schreiben ebenfalls leichte Koordinationsstörung, auch beim Sprechen. Meine Hände sind recht zyanotisch (zeigen einzelne rote und blaue Flecken) und fühlen sich kalt und feucht an. Ich empfinde eine gewisse Uebelkeit, aber keinen Brechreiz. Ich habe den Eindruck, dass meine Gefühle ganz flach geworden sind, aber sehr rasch ansprechen. Die Zeit scheint mir viel rascher als sonst vergangen. Mir ist es, als ob ich gar kein richtiges Gefühl mehr für den Ablauf der Zeit habe..... gewisse Kontaktschwierigkeiten, es gelingt mir auch nur mit Mühe, mich einigermaßen klar auszudrücken, da mir die Begriffe zerfließen wie auch die Worte entschwinden. Dennoch behaupte ich, ich könne mich im jetzigen Zustand in alle möglichen Seelenverfassungen Anderer einfühlen. Ich empfinde immer wieder, dass ich eigentlich nur dummes Zeug zum grössten Teil daherrede, und ich muss dann plötzlich schallend lachen deswegen, was mir meist recht unangenehm ist. Ich fühle mich etwas gedemütigt, dass mich das LSD so verändert hat. Ich fühle mich deutlich verändert und zwar im Sinne einer Karikierung meiner sonstigen Charaktereigenschaften... Irgendwo im Zimmer leuchten plötzlich einer oder mehrere helle Punkte zugleich auf, verschwinden entweder sofort wieder oder erst, nachdem sie rasch eine mehr oder weniger lange, meist gerade, aber auch gekrümmte Bahn beschrieben haben. Beim Blick ins Helle starke negative Nachbilder. Eine rote Kravatte erscheint eigentümlich flammend-rot mit grünlichem Rand. ... Als ich die Villa, um zum Mittagessen zu gehen, verlassen will, fällt mir ein, dass ich den Hausschlüssel vergessen habe. Kaum habe ich ihn geholt, so entdecke ich wiederum unter der Villa-Haustüre, dass ich den Füllfederhalter nicht bei mir habe. Ich hole auch diesen, weil ich dort noch die Mappe mit Akten für die Poliklinik liegen gelassen habe. Beim Gehen wieder das eigentümliche Schwebefühl. Ich habe auf einmal die Empfindung, ganz winzige Beine zu haben, kann aber doch Schritte von gewohnter Länge machen. Vor dem Kasino treffe ich mit einem Hauspfarrer zusammen und habe den Eindruck, er sehe mir an, dass es mit mir nicht mehr ganz richtig ist. Die Kolleginnen und Kollegen haben irgend etwas Starres, Automatenhaftes an sich. Mich überfällt von Zeit zu Zeit ein unwiderstehlicher Lachdrang, obwohl mir eigentlich gar nicht besonders ums Lachen ist und fast immer ohne besonders äusseren Grund, was mir sehr töricht vorkommt. Ich mache öfters recht läppische Bemerkungen. Ein klares Überlegen längerer Zusammenhänge ist mir nicht mehr möglich. Allerlei unzusammenhängende, sonderbare Einfälle folgen sich aufeinander, sind aber so unbestimmt, wie traumhaft, dass ich sie nicht behalten kann. Das Gesicht eines Kollegen erscheint mir rasch wechselnd ganz breit, dann wieder ganz schmal; auch beide Gesichtshälften verändern sich so unabhängig voneinander. Meine passive Ablenkbarkeit ist

sehr stark gesteigert. Ich schnappe bald da, bald dort ein Wort aus der Unterhaltung der andern auf, versuche einzuhaken, aber der Gedankengang kommt nicht in Schwung... Ich erblicke auf der andern Strassen-seite einen Portier des Burghölzli und überlege mir, ob der wohl beauftragt wurde, mich zu beobachten. Ich habe überhaupt den Eindruck, dass alle Menschen, die mir auf ein paar Meter nahe kommen, mich prüfend ansehen, was mir nicht sehr angenehm ist. Meine Bewegungen kommen mir ausgesprochen eckig und linkisch vor. Die Leute haben irgend etwas Lebloses, Puppenartiges, Maskenhaftes, Künstliches an sich. Gewisse Details in ihrem Gehaben kommen mir lächerlich, unaufrichtig vor, schauspielhaft aber schlecht. Ich finde es teils komisch, teils beunruhigend, dass die Leute offenbar nicht merken, dass ich nicht mehr ganz normal bin. Wie eine „Erleuchtung“ kommt es über mich, dass es im Grunde ganz egal ist, was man tut, man ändert am Lauf der Welt doch nichts.

Meine Schrift zeigt deutliche leichte Koordinationsstörungen; Schreibmaschinenschreiben geht nur mit recht vielen Fehlern, die Buchstaben auf den Tasten sehe ich viel kleiner als sonst... Als ich durchs Fenster schaue, sehe ich im Hause gegenüber — etwa 20 Meter weit weg — eine Frau, die aus dem Fenster zu mir hinschaut. Hinter dem Vorhang bei ihr scheint mir noch eine zweite Frau zu stehen. Ob mich die beiden wohl beachten? Mögen sie es tun.

In der Nacht während einer halben Stunde etwa ein gewisser Drang, aufzustehen und irgendwohin zu laufen, auch etwas suizidale Gedanken.“

DIE VERSUCHSERGEBNISSE BEI GEISTESKRANKEN

In der Tabelle haben wir die bei 30 Patienten durchgeführten Versuchstage und Dosierungen zusammengestellt. Das Untersuchungsmaterial setzte sich aus folgenden Krankheitsbildern zusammen:

- 10 Paranoide Schizophrenie
- 6 Katatonie
- 5 Hebephrenie
- 2 einfache Schizophrenie
- 2 Pfropfschizophrenie
- 1 Schizoide Psychopathie
- 1 Paranoid-, manisch-depressive Mischpsychose
- 2 Endogene Depressionen
- 1 Progressive Paralyse

Die Versuchsergebnisse sind schematisch zusammengestellt, wobei nur die wichtigsten und auffälligsten Symptome

berücksichtigt wurden. Während bei normalen Versuchspersonen auch geringfügige Erscheinungen eindeutig beobachtet und bewertet werden können, ist dies bei Geisteskranken völlig ausgeschlossen. Wechseln diese doch ohnehin täglich mehrmals in ihrer Stimmung und in den Angaben ihrer psychischen Erlebnisse.

Die Geisteskranken wiesen hinsichtlich des LSD eine bedeutend stärkere Resistenz auf, als die normalen Versuchspersonen. Bereits *Stoll* fand, dass die Symptomatik der LSD-Intoxikation bei Geisteskranken Patienten „im allgemeinen viel spärlicher und weniger farbig“ war als bei den Normalversuchen. Er erklärt dies zum Teil daraus, dass das Interesse am Versuch geringer war, dass es sich nicht um naturwissenschaftlich gebildete Versuchspersonen handelte, vor allem aber durch den schizophrenen Autismus und Negativismus, die Zerrfahrenheit und Dissimulationstendenz, die im allgemeinen die Selbstbeobachtung und die sorgfältige Berichterstattung verhiinderten. Eine endgültige Abklärung dieser Frage wurde auch durch unsere Versuche nicht möglich, doch schien uns, dass Negativismus und Zerrfahrenheit die Versuchsergebnisse nicht allzu stark beeinflussten. Gerade bei differenziierten Patienten, die über eine gute Selbstbeobachtungsgabe verfügen und über ihre seelischen Erlebnisse Auskunft geben, gelang es uns oft nicht, Angaben über spezifische, neu hinzugetretene und bisher unbekannte Zustandsbilder zu erhalten. Andererseits wurden autistische oder negativistische Kranke infolge einer gewissen Enthemmtheit, eines gesteigerten Rededranges und Mitteilungsbedürfnisses gelockerter und zugänglicher.

Es stellt sich die Frage, ob die Psychose an sich eine gewisse Resistenz gegen das LSD darstelle. Beispielsweise wäre es theoretisch möglich, — wenn auch als Arbeitshypothese vorläufig zu gewagt — dass die Geisteskrankheit durch einen gleichen oder ähnlichen Stoff erzeugt würde, der in bedeutend stärkerer Konzentrierung im Körper vorhanden sein müsste. In diesem Falle würde das in so geringen Dosen verabreichte LSD beim Psychotiker einen ungenügenden Reizzuwachs bilden, während es beim Normalen stark genug ist, um abnorme

psychische Erscheinungen hervorzubringen. Allerdings erwies sich die quantitative und qualitative Symptomatik der LSD-Intoxikation als unabhängig von der Schwere der Psychose. So erzielten wir mit relativ geringen Dosen bei einer schweren Katatonie (Fall 5) bedeutend eindrucklichere und auffälligere Veränderungen als beispielsweise bei einer blanden endogenen Depression (Fall 13).

VEGETATIVE SYMPTOME

Am auffälligsten und zeitlich zuerst auftretend waren bei unsern Versuchen an Geisteskranken die vegetativen Symptome, wobei wie schon früher gesagt, nie bedrohliche Zustände auftraten. Einzig in zwei Fällen bestand eine gewisse Kreislauf-Kollapsgefahr, sodass die Kur abgebrochen werden musste.

Es zeigte sich ein leichtes Schwächegefühl, Müdigkeit, Uebelkeit, Schwindel und Kopfschmerzen. Besonders typisch war ein von den meisten Versuchspersonen angegebenes „Krankheitsgefühl“, ferner ein oft genanntes „Katergefühl“, wie nach einem schweren Rausch, was auch von normalen Versuchspersonen häufig angegeben wurde. Sehr häufig wurde ein fader Geschmack im Munde empfunden, der verschieden gedeutet wurde: als Medikamenten- oder Säuregeschmack, Metallgeschmack, Geschmack nach faulem Wasser, Gasgeschmack oder Blutgeschmack. Die Kopfschmerzen erschienen meist erst nach abgeklungener LSD-Wirkung und wurden beschrieben als Druckgefühl in der Schläfengegend, Kribbeln, Brennen oder Rauschen im Kopf, Zuschrauben des Kopfes usw. Oefters trat Brechreiz auf, in drei Fällen kam es zu Erbrechen. Einmal zeigte sich eine deutliche Hypersalivation, mehrmals Druck in der Magengegend, Herzangst. Weitere Symptome waren: Kälte- und Hitzegefühl, Blässe des Gesichts und Akrozyanose. In 3 Fällen traten Wadenkrämpfe auf, in einem Fall wurden die Beine als bleischwer empfunden. Einmal sahen wir eine Urticaria, wobei allerdings nicht festgestellt werden konnte, ob diese dem LSD zugeschrieben werden

musste oder nicht. Gelegentlich kam es zu Schweissausbrüchen; Störungen in der Diurese, wie sie Stoll bei normalen Versuchspersonen zT. beobachtete, wurden nicht wahrgenommen. Der Appetit war im allgemeinen unverändert, zweimal trat Appetitlosigkeit auf, einmal Heisshunger. Pulsveränderungen waren selten und dann im Sinne einer Frequenzverlangsamung. Einmal wurde der Puls schwach und flatterhaft. Die Atmung war in zwei Fällen verlangsamt und mühsam. Der Blutdruck senkte sich im allgemeinen, blieb jedoch meistens im Rahmen der Norm; einmal trat eine Hypertonie auf. Die regelmässig durchgeführten Laboratoriumsuntersuchungen des Urins ergaben keine Veränderungen. Im Blutbild wurden anfänglich in zwei Fällen leicht toxische Veränderungen festgestellt, die jedoch nicht regelmässig auftraten, sich nach zwei Tagen wieder verloren und nicht mit Sicherheit auf die LSD-Wirkung bezogen werden können.

NEUROLOGISCHE SYMPTOME

Von Seiten der Hirnnerven wurden keine objektiven Veränderungen festgestellt. In einem Fall trat ein horizontaler Nystagmus auf. Gelegentlich wurde ein leichter Tremor der Hände, häufiger ein Zittern der Augenlider bei Lidschluss beobachtet. Sensibilitätsstörungen wurden in einem Falle festgestellt, wobei die Versuchsperson scheinbar jegliches Gefühl für Berührungs- und Schmerzreize, sowie für die Empfindungen Warm und Kalt verloren hatte. Es handelt sich um eine in sich selbst versunkene, verschrobene Schizophrene, deren Angaben unzuverlässig sind. Weiter wurden Zuckungen im Gesicht beobachtet, einmal traten Zuckungen am ganzen Körper auf. Das häufigste Symptom war, wie bei normalen Versuchspersonen, eine leichte Ataxie, Unsicherheit beim Gehen und Stehen (breitspuriger, schwankender Gang), wobei der Romberg'sche Versuch oft angedeutet positiv wurde. Auch hier zeigten sich die Symptome jedoch bedeutend schwächer als bei normalen Versuchspersonen. So wurde nie ein stark positiver Romberg beobachtet, ebensowenig zeigten sich grobe

Störungen bei den Zeigerversuchen; Danebengreifen oder Danebenlegen von Gegenständen wurde nie beobachtet, die Sprache wurde nur in einem Fall undeutlich. Hingegen traten motorische Störungen auf in dem Sinne, dass die ausgeführten willkürlichen Bewegungen ungenau und unkoordiniert ausfielen. Auch zeigte sich häufig eine gewisse motorische Unruhe: die Versuchspersonen gingen dauernd auf und ab, setzten sich und standen wieder auf, nahmen Gegenstände in die Hand und legten dieselben wieder weg usw. In einem Fall wurden athetotische Bewegungen beobachtet, was eventuell auf eine diencephale Mitbeteiligung beim LSD-Rausch hinweist. In diesem Zusammenhang muss wohl auch das bei sozusagen allen Versuchspersonen beobachtete „Zwangslachen“ gebracht werden, das in den meisten Fällen das auffälligste Symptom der LSD-Vergiftung darstellte und auch bei normalen Personen im Vordergrund stand. Es handelt sich dabei nicht um ein Lachen, das allein auf eine besondere euphorisierende Wirkung des LSD zurückgeführt werden könnte, sondern vielmehr um ein unwillkürliches, von der seelischen Grundstimmung unpropotioniert abhängiges, zwangshaftes Grimassieren, das subjektiv und objektiv als ein ungewolltes „Schmunzeln“ empfunden wird, wobei die Grundstimmung allerdings nicht unbeeinflusst bleibt. So kann ein geringfügiger äusserer Reiz, oft inadäquater Natur, aus diesem zwangshaften „Verziehen der Mundwinkel“ einen Lachkrampf auslösen.

In einigen Fällen traten Störungen der Tiefensensibilität auf. Schweregefühl, Schläffheit, Kraftlosigkeit, Muskelkater und ähnliche Störungen des Körpergefühls wurden mehrmals empfunden. Eine Versuchsperson hatte das Gefühl, ihr Kopf sei angeschwollen, eine andere Versuchsperson, ihr Kopf und ihre Arme seien verändert und vergrössert.

Wir liessen auch Schriftproben anfertigen, wobei keine groben Veränderungen bemerkt wurden. Das Reflexbild wies selten Störungen auf; in einigen Fällen zeigte sich eine Steigerung der PSR mit Verbreiterung der reflexogenen Zone, in einem Falle waren sämtliche Reflexe vorübergehend gesteigert.

Veränderte Pupillenreaktionen wurden nicht festgestellt; in einem Falle beobachteten wir Doppelsehen.

STÖRUNGEN DER WAHRNEHMUNG

Stoll fand bei seinen Versuchen an Normalpersonen wie wir u. a. häufig eine Bereitschaft zu illusionistischer Verknüpfung der Umgebung, ferner synästhetische Reaktionen, perspektivische Fehlleistungen und Pseudohalluzinationen, während die Symptomatik bei seinen Kranken auch in dieser Beziehung spärlich war. Bei unsern Untersuchungen bestätigten sich diese Befunde. Darüber hinaus beobachteten wir keine Patienten mit Halluzinationen, die nur durch das LSD hätten bedingt sein können. In einigen Fällen halluzinierten die Patienten, doch wurden diese Halluzinationen immer in das vorbestehende Krankheitsbild eingegliedert und konnten nicht als spezifische Giftwirkungen davon abgetrennt werden. Unterschiede im Hell- oder Dunkelmilieu wurden nicht festgestellt. Hingegen vermuten wir, dass der LSD-Rauschzustand in einigen Fällen als auslösender Reiz zu den Sinnestäuschungen wirkte. Bei einigen Versuchspersonen zeigte es sich nämlich, dass die Halluzinationen während der LSD-Kur gehäuft auftraten. Bei einer Versuchsperson jedoch, die vor der Kur fast täglich visuelle und akustische halluzinatorische Erlebnisse hatte, verschwanden dieselben vorübergehend unter der LSD-Wirkung. Eine Versuchsperson sah während der LSD-Wirkung Geister in der Luft und sprach dauernd mit denselben. Diese Versuchsperson war auch völlig unfähig, vorgezeigte Farben zu erkennen und zu benennen, oder Farbunterschiede anzugeben. Allerdings zeigte es sich auch hier, dass diese Symptome der Geisteskrankheit und nicht der LSD-Intoxikation zuzuschreiben sind. Eine weitere Versuchsperson gab an, nachmittags beim Abliegen mehr Stimmen zu haben als sonst und äusserte visuelle Halluzinationen, die sie angeblich nie hatte: verschiedene Gestalten die sie nicht näher beschreiben könne, das schreckliche Gesicht eines Teufels, von schillern-dem Schwarz mit helleuchtenden Augen, verschiedene Gesich-

ter von Götzen wie Chinesen mit langen Schnäuzen, nicht farbig, sondern nur weiss-schwarz; eine einzelne Hand mit 4 Fingern, daran lange Krallen. Die Versuchsperson brachte diese Halluzinationen mit ihrem Wahnsystem in Beziehung und erklärte, eine Stimme habe ihr gesagt, dies alles werde ihr von einer Nebenpatientin gezeigt. Auffällig an diesem Erlebnis war lediglich, dass die Versuchsperson seit längerer Zeit keine visuellen Halluzinationen mehr gehabt hatte. — Illusionistische Verkennungen, Farbhalluzinationen und dergleichen wurden nicht beobachtet, in zwei Fällen fielen ungenaue Farbangaben auf. Auch die Versuche, suggestiv Sinnes-täuschungen zu erzeugen, blieben ohne positive Ergebnis. Ebenso fielen die Versuche im Dunkelmzimmer meist negativ aus. Eine einzige Versuchsperson halluzinierte bei dieser Gelegenheit stärker als im hellen Saal, jedoch deutlich schizophoren.

STÖRUNGEN DER BEWUSSTSEINSLAGE UND DES PERSÖNLICHKEITSGEFÜHL

In drei Fällen traten eigentliche Verwirrheitszustände ein, wobei es einmal bei einer Dosierung von 20 gamma zu einem Dämmerzustand kam (Fall 20). Beim gleichen Fall trat auch eine starke motorische Unruhe, Singultus und Urticaria in Erscheinung, was wohl auf eine besonders individuelle Indisposition zurückgeführt werden kann. In einem andern Fall (15) trat bei 90 gamma LSD und bei Fall 17 mit 20 gamma eine leichte Verwirrtheit auf. Im allgemeinen wurde bei den angeordneten Dosierungen keine schwere Beeinträchtigung des Bewusstseins festgestellt, häufig jedoch fühlten die Versuchspersonen eine leichte Benommenheit im Sinne des oben bereits erwähnten Rauschgefühls. Die bei den Normalpersonen häufig angetroffene Enthemmtheit äusserte sich bei unsern psychotischen Versuchspersonen bedeutend weniger eindrucklich. Nur in wenigen Fällen wurde ein übertriebener Rededrang festgestellt. Hingegen wirkte sich die Enthemmtheit in einigen Fällen dahin aus, dass die Versuchspersonen in massloser

Weise zu schimpfen begannen und gegen Aerzte und Pflegepersonal ausfällig wurden. Es handelte sich aber jedesmal um Patienten, bei denen solche Affektausbrüche schon nüchtern öfters beobachtet werden. — In einem Fall (Fall 19) traten Depersonalisationserscheinungen auf, ferner Hang zum Perseverieren.

Die Grundstimmung war vor der LSD-Verabreichung in 9 Fällen an den Versuchstagen ausgesprochen depressiv, in 7 Fällen euphorisch; während des LSD-Rausches wurden bei diesen 16 Fällen keine eigentlichen Stimmungsschwankungen beobachtet. Es handelte sich dabei um Patienten, bei denen diese Stimmungslage bereits im Habitualzustande, also unabhängig von der LSD-Kur bestand. Die restlichen 14 Fälle zeigten ein wechselndes Verhalten, wobei jedoch nicht von einer spezifischen LSD-Wirkung gesprochen werden kann. Kleinere Stimmungsschwankungen sind ja bei Geisteskranken die Regel und es wäre zu weit gegriffen, wollte man aus einem kurzen vorübergehenden Stimmungsumschwung eines Patienten auf die Wirkung des LSD Bezug nehmen. Bei diesen 14 Kranken waren 3 in ihrer Grundstimmung eher ausgeglichen und unauffällig, 2 beinahe dauernd erregt, während 9 reizbar waren, sich jedoch zeitweise beruhigten.

EINTRITT DER LSD-WIRKUNG UND WIRKUNGSDAUER

Schon bei normalen Versuchspersonen zeigte es sich, dass die Dauer biszum Eintritt der ersten neurovegetativen oder psychischen Symptome individuell verschieden war. Die ersten Anzeichen traten frühestens nach ca. $\frac{1}{2}$ Stunde, spätestens nach 2—3 Stunden auf. Bei unsern Versuchen an Geisteskranken fanden wir ähnlich Verhältnisse, wobei infolge der schon bei Normalen beobachteten Unterschiedlichkeit keine genauen Vergleichsmöglichkeiten gegeben sind. Das gleiche gilt bezüglich der Wirkungskdauer des LSD-Rausches. Bei einzelnen klangen die Symptome sehr schnell ab, bei andern dauerten sie bis in den Nachmittag hinein. *Im allgemeinen hatten wir den Eindruck, dass die LSD-Intoxikation bei unsern psychotischen*

Versuchspersonen blander verlief als bei den Versuchen an Geistesgesunden. So konnten wir nur in wenigen Fällen Nachwirkungen leichter Art (Uebelsein, Kopfweh) finden, während dies bei den normalen Versuchspersonen bedeutend häufiger der Fall war.

THERAPEUTISCHE WIRKSAMKEIT

Unsere Untersuchungen liessen keine endgültigen Rückschlüsse auf die Brauchbarkeit des LSD als psychiatrisch anwendbares Therapeutikum zu. Der Zeitraum der Beobachtung war zu kurz, um irgendwelche Dauererfolge feststellen zu können. Auch muss hier betont werden, dass die Auswahl der Versuchspersonen — wie bereits eingangs erwähnt, wurden vor allem Geisteskranke für die Versuche herangezogen, bei denen die übliche Therapie erfolglos geblieben war — keine bedeutenden therapeutischen Effekte erwarten liess. Die teilweise sehr ausgesprochene euphorisierende Wirkung des Mittels an gesunden Versuchspersonen liess die Vermutung aufkommen, es könnte bei depressiven Zuständen in ähnlicher Weise anwendbar sein, wie beispielsweise die Opiumkuren. Aus diesen Gründen gaben wir 5 depressiven Patienten während mehrerer Tage kleine, täglich ansteigende Dosen des LSD und beobachteten besonders die Veränderung der Stimmungslage. Lediglich zwei Versuchspersonen wurden etwas zugänglicher und gelockerter. Eine eigentliche, über die täglichen Schwankungen hinausgehende Besserung der Depression war jedoch in keinem der Fälle zu beobachten. Hingegen wurden unsere depressiven Patienten im Rausche häufig noch depressiver, womit unsere Ansicht, das LSD bewirke vor allem eine Verstärkung der bereits bestehenden Stimmungslage, bestätigt wurde. Bei den hypomanischen oder euphorischen Versuchspersonen jedoch imponierte das LSD als euphorisierendes Medikament.

Die bei gesunden Versuchspersonen so überaus stark empfundene seelische Wirkung führte zu der Vermutung, der LSD-Rausch könnte in der Psychiatrie im Sinne einer Schock-

behandlung angewendet werden. Es würde sich in diesem Falle nicht um die gleiche Schocktherapie handeln, wie wir sie in der Psychiatrie anzuwenden pflegen (Insulin- und Elektroschock, Schlafkur), sondern um eine Schockwirkung auf medikamentös-pharmakologischer Grundlage. Die Stärke des seelischen Erlebnisses sollte beim Geisteskranken den therapeutischen Effekt erzielen. Diese Frage muss immer noch als unabgeklärt betrachtet werden. Bei der von uns angewandten Dosierung sprachen die Geisteskranken psychisch nur ungenügend an. Es ist nicht ausgeschlossen, dass mit einer bedeutend höher angesetzten Dosierung stärkere seelische Erschütterungen erzeugt werden könnten, doch kann dabei die Gefahr erheblich somatischer, vor allem vegetativer Störungen noch nicht abgeschätzt werden.

DIAGNOSTISCHE VERWERTBARKEIT

Um in diagnostischer Hinsicht verwertbare Resultate zu erzielen, wären Versuche an einem grössern Krankengut notwendig. In quantitativer Hinsicht, d. h. bezüglich der Resistenz gegenüber dem LSD konnten wir bei den verschiedenen Krankheitsbildern keine differential-diagnostisch brauchbaren Unterschiede finden. Es zeigte sich, dass sowohl hebephrene wie paranoide Schizophrenien, schwerste Katatonien und auch andere Psychosen, wie manisch-depressives Irresein und ein Fall von progressiver Paralyse, ganz unterschiedlich und uneinheitlich reagierten. Die stärkste Resistenz zeigte letztgenannte Erkrankung, bei der eine Höchstdosierung von 280 gamma erreicht wurde, ohne dass schwere Symptome auftraten. Im allgemeinen erwiesen sich die chronischen Zustandsbilder etwas resistenter, doch war dies nicht durchwegs die Regel, sodass von einer eigentlichen Parallelität zwischen Krankheitsschwere und Dosierung nicht gesprochen werden kann.

In qualitativer Hinsicht zeigten sich insofern gewisse Befunde, als die Persönlichkeitsveränderungen im jeweiligen Sinne des bereits vorbestehenden Krankheitsbildes verstärkt

wurden. So wirkte zB. die hebephrene Versuchsperson im LSD-Rausch noch deutlicher hebephren, der Katatone noch stärker kataton. Das LSD erzeugte bei den meisten Versuchspersonen einen Zustand, den wir als „Karikatur“ der eigenen Persönlichkeit, bezw. der Psychose bezeichnen möchten. Diese Eigenschaft des LSD zeigte sich schon und besonders deutlich bei den Versuchen an Normalpersonen und es liesse sich hier die Frage aufwerfen, ob der LSD-Rausch als „Persönlichkeitstest“ verwertbar wäre, was allerdings an grösseren Versuchsreihen abgeklärt werden müsste (*Rothlin*; vgl. auch *Stoll*).

ZUSAMMENFASSUNG

- 1) Lysergsäurediäthylamid ist ein Stoff, der bei Normalpersonen in Mengen von 20—30 Gamma (0,00002—0,00003 g) einen Rauschzustand im Sinne eines akuten exogenen Reaktionstypus bewirkt.
- 2) Es wurden in Fortsetzung der Untersuchungen von *Stoll* 197 neue LSD-Versuche bei 30 geisteskranken Probanden durchgeführt, dazu 7 Kontrollversuche an normalen Versuchspersonen.
- 3) Die Geisteskranken wiesen hinsichtlich des LSD eine bedeutend stärkere Resistenz auf als die normalen Versuchspersonen. Auch die Verträglichkeit des LSD scheint durchschnittlich bei Psychotikern besser zu sein als bei Gesunden. In 19 von 30 Fällen betrug die von uns verabreichte Höchstdosis LSD 100 Gamma und mehr, in einem Fall 280 Gamma.
- 4) Im Vordergrund der LSD-Vergiftung bei Geisteskranken standen vegetative Symptome (Schwächegefühl, Müdigkeit, Uebelkeit, Schwindel, Kopfschmerzen, Krankheitsgefühl, Katergefühl, Parästhesien, Hypersalivation, Schweissausbrüche, Kreislaufstörungen u. a. m.). Neurologisch wurden gelegentlich motorische und ataktische Störungen beobachtet (in einem Fall athetotische Bewegungen, häufig Zwangslachen, was eventuell auf eine diencephale Mitbeteiligung hinweist).

- 5) Die Störungen der Wahrnehmung, der Bewusstseinslage und des Persönlichkeitsgefühls waren bei den Geisteskranken weniger deutlich als bei den Geistesgesunden; auch verlief die LSD-Intoxikation hinsichtlich Eintritt der LSD-Wirkung und Wirkungsdauer blander als bei den Versuchen an Normalpersonen.
- 6) Die therapeutische Wirksamkeit konnte nicht endgültig abgeklärt werden. In einzelnen Fällen wurde eine euphorisierende und enthemmende Wirkung des LSD festgestellt, in andern Fällen wurde eine vorbestehende Depression verstärkt.
- 7) Eine differentialdiagnostische Verwertbarkeit des LSD besteht auf Grund unserer Versuche nicht. Die Abklärung dieser Frage dürfte nur an grösserem Krankengut Resultate ergeben.
- 8) Zukünftige Versuche mit LSD sollten sich vor allem mit der Frage der Schockwirkung befassen, von der eventuell eine therapeutische Wirkung zu erwarten wäre, wobei einerseits höhere Dosen angewandt werden müssten, denen andererseits vor allem vegetative Störungen (Kollapsgefahr) eine Grenze setzen.
- 9) Auf Grund der Resistenz der Geisteskranken gegenüber dem LSD wurde arbeitshypothetisch die Frage aufgeworfen, ob Psychosen durch einen dem LSD ähnlichen Stoff erzeugt würden. Auch in dieser Richtung dürften weitere Untersuchungen interessante Resultate zeitigen.

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ON THE INITIAL IMPAIRMENT OF
CONSCIOUSNESS FOLLOWING ELECTRIC
CONVULSIVE THERAPY

Preliminary Communication

BY

VILLARS LUNN & ELLI TROLLE

The principle on which shock therapy, as applied to psychotic and neurotic patients, is based is an artificially produced, transient alteration of the consciousness—i.e. an alteration in the intensity of the consciousness in patients whose consciousness is otherwise clear. The various types of shock treatments are all characterized by an initial loss of consciousness, in some cases accompanied by eclamptic phenomena. The initial coma is followed by a period of relatively short duration during which the patient passes through all the stages from complete loss of consciousness to complete clarity of consciousness. In this period a considerable psychomotor unrest is frequently observed as well as a transient change in the emotional tone, just as the patient often shows signs of suffering from hallucinations and frequently seems to be in a state of anxiety—bordering on panic. The initial coma is thus followed by a state of turbid consciousness of varying duration; in most cases complete amnesia will be found for this condition.

This course of events repeats itself in all kinds of shock. Consequent upon the reestablishment of complete consciousness a more lasting change, chiefly in the mood and the psychomotor activity, is observed in some cases. This is the result which is aimed at by the therapy. In other patients the

shock may be followed by a usually transient amnestic syndrome. This represents the most serious complication in connection with the therapy.

The treatment of shock therapy in the literature has hitherto chiefly aimed at the two latter phenomena: the therapeutic effect and the postictal amnestic syndrome. The initial impairment of consciousness, on the other hand, has to a surprisingly small extent been subjected to theoretical treatment. The reason for this is probably that the post-comatose state of confusion appears to be identical with the postictal syndrome of the generalized epileptic fit, which is probably considered to have been treated in all details.

There is, however, no doubt that through the experimentally produced loss of consciousness and the consequent rapidly disappearing impairment of consciousness, as it manifests itself in the patients who have been subjected to shock treatment, we have been given a psychological research object of considerable theoretical interest.

When studying the psychopathology of conditions characterized by impairment of the consciousness we have hitherto had to resort to such conditions as the postictal confusion after head-traumata, the toxic or infectious delirious conditions, the sopor connected with intracranial diseases, etc. Compared with these conditions the postcomatose impairment of consciousness after the experimentally produced shock presents the following advantages from a theoretical point of view:

(1) There is a possibility of obtaining knowledge of the mental structure of the patient *before* the manifestation of the pathological condition which it is desired to analyze,—without which knowledge it would be impossible to evaluate a long series of elements in the altered state of consciousness: content of memory, retention, orientation in time, type of visual experience, etc.

(2) The time elapsing between the total loss of consciousness and the complete clarity of consciousness is short, usually less than two hours, which makes it possible in practice

to perform a *continuous* recording of a number of elements of the consciousness during the gradual reestablishment of these elements—and of the chronological order of the return of the individual elements.

(3) It is possible in practice in the course of a short time to produce a considerable material—which is of particular importance if the purpose is to compare the value of various experimental methods.

(4) Experiments can be performed repeatedly with the same patient, and this offers a possibility of an evaluation of individual differences in the reaction of the patients to the noxa.

(5) The fact that the time at which the shock is to occur can be determined in advance presents an opportunity of performing a more exact study, especially of the mechanism of the retrograde amnesia, than in any other state of disturbed consciousness.

On the basis of the considerations stated we decided at the *Psychiatric Clinic of Rigshospitalet*, Copenhagen, to try to perform a psychological analysis of the postcomatose state of confusion in patients treated with electric shock.

Employing as the basic psychological principle for our work the usual classification in separate qualities or elements of the consciousness: attention, perception, autopsychic and allopsychic orientation, content of memory, retention, etc., we drew up a plan for our work in the form of the following questions: (1) What is the relation between the resistance and vulnerability, respectively, of the individual elements of the consciousness towards the general reduction of the mental tension which manifests itself after the electric shock? (2) In which chronological order will the individual elements of the consciousness be reestablished during the period from total loss of consciousness to complete mental clarity? Is it possible on the basis of the sequence to draw any conclusions as regards the psychological connection between the individual elements?

As the investigation proceeded we soon realized that this delimitation of the problem was far too narrow. Moreover, the method used by us proved on several points to be inadequate for the purpose in question. But what was even more important, we rapidly realized that the fundamental principle on which we had based the investigation: the classification according to the traditional "elements" of the consciousness and the evaluation of the degree of reestablishment of the latter, did not seem to be a suitable method for the purpose of analyzing the psychopathology of the impairment of consciousness.

The mental activities which manifest themselves, e.g. in the allopsychic orientation, the ability to name objects, body orientation, etc., must be supposed to be based on more elementary or fundamental mechanisms, which do not seem to be adequately elucidated by the usual questions as regards orientation or the attention and perception tests. Such questions and tests present a momentary picture of the perfectibility of the patient within a fairly wide, but to some extent rather arbitrarily chosen field, but it does not yield any description of the fundamental mental disturbances.

It would here be necessary to develop a more refined technique than the one usually applied to the evaluation of the degree of a somnolent state.

The present investigations, the most important results of which we shall report in the following, should thus merely be considered a preliminary, rough orientation, the chief aim of which is to point out the theoretical problems which may be elucidated by investigations of this kind, and to draw attention to the spheres in which a more differentiated experimental technique will be particularly necessary if a more thorough knowledge of the psychopathology of the state of impaired consciousness is to be obtained.

METHOD

These preliminary investigations have been based on the following plan: 10 minutes, 30 minutes, and 60 minutes after the shock the patient has been given a series of questions and tasks for the purpose of elucidating the following elements of consciousness: autopsychic and allopsychic orientation, body orientation, attention, apperception, content of memory, retention, ability to name objects, arithmetical ability, etc. The questions and tasks, which were absolutely identical from shock to shock, could generally be answered and performed by a person of normal consciousness in the course of 3-4 min.

By thus attempting a "transverse" evaluation of a number of mental faculties in the same patient at different stages of the gradual reestablishment of consciousness, we aimed at an elucidation of the relation between the vulnerability of the individual qualities or elements and, if possible, of their mutual psychological relationship.

However, an examination carried out on this principle will, even when simple tests are used, take a rather long time when applied to a somnolent patient as compared with the corresponding time with a person in a state of normal consciousness. In practice we have adopted the method that the patient has been granted 15 seconds for each question. If after this period no reply has been obtained, the test has been considered to be negative. Nevertheless the first examination, i.e. 10 min. after the shock, lasted as regards about 75 per cent. of the patients between 5 and 10 min., and as regards about 20 per cent. of the patients more than 10 min. This means that the patient's condition will have time to change perceptibly between the first and the last tests within the same group, for which reason a comparison between the results of two different examinations will only be of a conditional validity. This inherent weakness of the method is inevitable if more than one element of the consciousness is to be studied in each patient. It may be overcome by reducing the examination to a continuous observation of the gradual reestablishment of

a single or very few elements in one group of patients and by comparing this chronological order with the result of a similar continuous recording of the reestablishment of another or a number of other elements in another group of patients. In the course of the discussion we shall return to this fundamental question of method.

The procedure during the present investigation has been as follows: Before the shock treatment is commenced the patient is submitted to a number of psychiatric tests. In this way it is possible to form a picture i.a. of his content of memory and after the shock to check his answers to a number of ordinary questions as to orientation. One hour before the shock the patient is shown a picture (from a picture-lotto), 5 min. before the shock another picture is shown to him. He is asked to memorize the pictures, and it is explained to him that these pictures will later on be shown to him among a number of similar pictures, and that he will be asked to pick out the two pictures previously shown to him. The aim is to obtain an idea as to the extent of a possible retrograde amnesia.

Exactly 10 min. after the shock the first series of questions is commenced and, irrespective of the duration of the first examination, it is repeated exactly 30 min., 60 min. and 120 min. after the shock. By means of a stop watch the duration of each examination is ascertained. The patient is granted 15 sec. for answering each question. If the latent period is longer, the result is considered to be negative, the same applies if, within the same period, the patient states that he "does not remember"—which is frequently the case. For *Bourdon's* test for attention and for the picture-description tests the patients are, however, granted up to one min. and for the subtraction test up to half a min.

The questioning of the patients after 10, 30, and 60 min. proceeds almost uniformly from examination to examination, most of the questions being identical. An exception is formed by the subtraction sums and the tests for retention of figures, which differ from one series of questions to the next belong-

ing to the same shock, but are identical from one shock to the next, and by the material for the picture-description tests, which vary both as regards the different examinations in one series and as regards different shocks in the same patient.

The examination performed two hours after the shock only comprises the questions which the patient during the previous examinations either failed to answer or to which he gave an incorrect answer. At this time a retention test according to *Ranschburg's* word-pair method is performed, a new series of words being used for every new shock treatment of the same patient.

As regards the *individual tests* we have for these preliminary investigations used the following traditional orientation tests:

For judging the *autopsychic orientation* the patient was asked his name, age, marital state, and residence.

As regards the *allopsychic orientation* the patient is asked his present whereabouts, month and day of the week, and the duration of his stay in hospital.

For the evaluation of the *content of memory* we have used place of birth, name of school, name of siblings and father, and if the patient has no siblings, the names of some of his teachers. Finally we have asked about the year and date of the occupation of Denmark by the Germans.

As a *retention test* we have for the first three groups of questions used the retention of a single figure. We have used figures with four digits and distraction of attention with a subtraction test of the type 55 minus 18. Both the immediate retention and retention after distraction has been recorded. New figures and sums have been used for each group of tests after one shock,—but identical tests have been used for all the patients.

As mentioned, we have tried to illustrate the extent of a *retrograde amnesia*, if any, by showing the patient two pictures from a picture-lotto 60 min. and 5 min., respectively, before the shock, and by presenting him after the shock with these two pictures together with five others from the same

lotto and asking him to pick out the two previously shown pictures. The pictures were of simple and presumably neutral objects, as e.g. a watering pot, a drum, etc.

As a *gnostic test* we have used the names of objects, the patient being shown a fountain pen, a safety pin, and a match-box and asked the names of these objects. The patient has further been asked to name the colour of the wall.

The body-orientation and the right-left orientation we have tried to illustrate roughly by a crossed pointing test: "Point with your right forefinger at your left ear." We have tested for finger agnosia or amnesia as to the names of the fingers by telling the patient to close his eyes and then, taking hold of his fourth finger on the left hand, asking him the name of the finger touched.

The attention test applied has been a slightly modified type of Bourdon's crossing-out test. The time consumed in solving the problem is observed and so is the number of times the instruction must be given in order to be understood by the patient.

As a combined *attention and perception test* we have finally used a description of a picture shown to the patient. We have had to compose a pictorial material for the purpose as we had to use a new picture for each group of tests after a shock and for each new shock in the same patient. The results of the tests have been classified as very good, when the patient has understood the point of the picture and has spontaneously described a number of details; fairly good, when the description is ample, but does not disclose an understanding of the point; and, finally, inferior, when the patient has failed to give any description whatever or has only been able to mention inessential details in the picture.

In conclusion the chart has been provided with a note as to the patient's mood, affective state, and psychomotor reactions during the group of tests in question.

MATERIAL

The present preliminary investigations have been carried out on the basis of 66 shocks, the patients subjected to the shocks being 10 women and 11 men. In 5 cases the patient was examined after a single shock only, in 1 patient the examination was repeated after 7 consecutive shock treatments, in the remaining the examination was based upon from 2 to 6 shock treatments.

The *diagnosis* was in 14 cases *depressio mentis endogenica*, in the remaining cases *depressio mentis psychogenica* or the manic state of a manic-depressive psychosis.

The *initial dosis* has usually been 120 M.A.S. If no convulsions have been obtained with this dosis, it has been increased to 170 or 210 units, respectively. In 3 cases it was necessary to give more than 300 units.

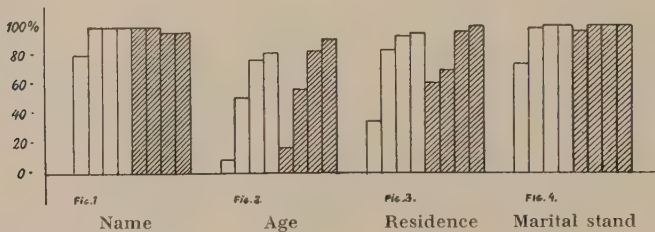
Irrespective of the small number of cases of which our material consists, we have tried to classify our material according to sex, diagnosis, dosage and according to the number of the shock. As might be expected, the material is not large enough to justify such a classification.

In one field only it was possible to ascertain a connection between a known factor which may be controlled and the degree of the postcomatose impairment of consciousness: the somnolence is deeper and the turbidity of the consciousness of a longer duration after convulsions than after petit mal seizures. For this reason it has been necessary to divide the material into two categories: i.e. convulsive states and minor seizures. The difference in degree and duration of the initial impairment of consciousness subsequent to convulsions and petit mal seizures, respectively, is of course in no way surprising. But it serves to render more concrete the practical therapeutical problem as to the optimum shock dosis and the therapeutical importance of obtaining convulsions, problems which have not yet been solved.

RESULTS

With due regard to the reservation which is a natural consequence of the smallness of the material we have tried in the following to represent the results of the investigations in the form of graphs.

The bar graphs represent the number of correct and good answers in per cent. of the total number of shocks. The unhatched columns represent the convulsive cases and the hatched columns the cases of petit mal seizures. The first column denotes the "plus percentage" in the first group of questions, i.e. 10 min. after the shock, the second column denotes the group of questions 30 min. after the shock and so on.



Figs. 1-4 represent the results of the *autopsychic orientation tests*, i.e. questions as to name, age, residence, and marital state. It is seen that after 30 min. and at the time of the subsequent tests all the patients were able to reply correctly to the questions as to name and material state. With regard to the patients with petit mal seizures this is the case already when 10 min. have elapsed since the shock, while with regard to the patients with convulsive states it holds that about 20 per cent. at this time are unable to state their name correctly and about 25 per cent. are unable to answer the question about their marital state.

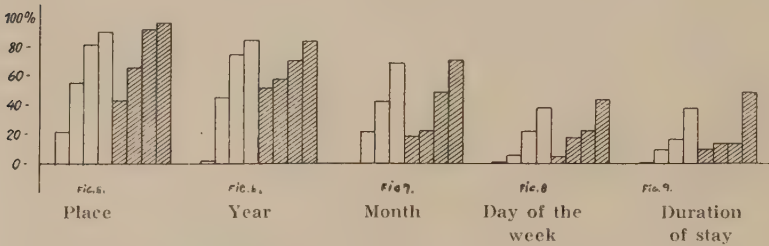
The corresponding figures are considerably lower with regard to the questions as to age and residence; 10 min. after the shock only 9 per cent. of the convulsive cases are able to state their age correctly and 35 per cent. to state their re-

sidence correctly. With regard to the patients with minor seizures the corresponding figures were 17 and 61 per cent., respectively. 30 min. after the shock only half of the convulsive cases can remember their age and even two hours after the shock about 20 per cent. of all the patients are unable to state their age or state it incorrectly.

It is thus seen that as regards "personal data", name and marital state appear to possess the greatest resistance towards the general impairment of the consciousness, while particularly the question of age is very vulnerable. This is not surprising. Also to the intact, lucid consciousness certain invariable concepts, as e.g. a person's name, are more solidly established and more easily reproducible than other, more variable personal data, such as age and residence. It is not, however, without interest that here we have obtained an opportunity of finding an—of course approximate—*numerical expression* of the difference in the extent to which various data or concepts are established in the consciousness. When verified by means of a larger material, such an exact observation of the different degrees of stability with which the various concepts are established in the consciousness would represent a concrete starting point for an analysis of the psychological identity or incommensurability of these concepts.

It applies to all these tests, as to all the following ones, that the possibility should be taken into consideration that the difference between the number of correct answers to the different questions within the same field of concepts may be due to the fact that the questions are not equally easily *comprehended*—that, in other words, the variation is caused by defective apperception and not by an expressive defect or a failing ability to mobilize the concepts. The technique used for the present preliminary investigations has not to a sufficiently high degree been aimed at a fundamental discrimination between impressive and expressive psychological mechanisms. This is one of the points on which a revision of the examination technique will be necessary if further progress along this line is to be made.

Such questions as: "What is your name?—How old are you?—Where do you live?—Are you married or unmarried?" do, however, to an immediate consideration appear to be equally difficult. It seems to be highly probable that the variation in the number of correct answers ascertained with regard to these questions is determined by differences in the ease with which such concepts are mobilized and not by disturbances in apperception.



We shall now consider the results of the *allospsychic orientation tests*. These results are graphically reproduced in figs. 5-9.

The *orientation in space* (fig. 5) was fully intact 10 min. after the shock in 21 per cent. of the convulsive cases and in 43 per cent. of the patients with minor seizures. Besides, 19 and 22 per cent., respectively, were able to reply that they were in a hospital, but were unable to state which hospital. 30 min. after the shock the number of correct answers had risen to 55 and 65 per cent., respectively. 60 min. after the shock to 81 and 91 per cent., respectively, and finally 120 min. after the shock to 90 and 96 per cent., respectively, to which figures may be added 5 and 4 per cent., respectively, in which the answer has been "hospital". The course of the graph thus gives a fairly good representation of the gradual restitution of the perfectibility of the patients within this sphere. It does not, however, yield any immediate information as to the nature of the integrating psychological elements and mechanisms.

The first condition of a correct answer to an orientation question is that the question has been correctly understood.

The next condition is that the patient perceives the surroundings correctly, and that he is able to mobilize the name corresponding to the conception which the visual impressions produce in his mind. But it may also be possible to obtain a correct answer if the patient simply *remembers* where he is, or, perhaps even better, "*knows*" where he is.

When a person wakes up in the morning after having slept for the first time in a new room, it may happen that he suffers a massive disorientation as to place—he has not the faintest idea as to his whereabouts. During the following seconds orientation will be restored, either by the memory of certain events from the preceding days appearing and reestablishing the broken continuity of the consciousness or by the sight of certain objects in the surroundings—an unpacked trunk, a picture on the wall—, which suddenly brings about the correct orientation in space. The most frequent experience is, however, that orientation in space is reestablished immediately, simultaneously with the consciousness—just as it is the usually permanent background of our experiences when awake.

The object of these somewhat obvious considerations has been to indicate some of the psychological mechanisms which must be assumed to be an integral part of the category of the consciousness which is usually known under the simplified designation "orientation in space", and of the condition of which we want to be informed when we put the question, "Where are you now?" to the patient.

A number of these mechanisms may to some extent be evaluated on the basis of the simplified examination technique used for the purpose of the present investigations. If the patient answers e.g. "Yes, where am I?" or "At home," or "Where I am?—I do not know,"—it is obvious that the meaning of the question has been understood. If the reply—the patient having looked about inquiringly—is: "You're a doctor, aren't you? Then I suppose I am in a hospital," both question and surroundings have been perceived correctly. If finally the

reply is a prompt "In hospital," it is evident that the immediate orientation in space has been reestablished.

It is, however, obvious that a *periodical* questioning, as it has been practised for the purpose of our investigation, does not offer any possibilities of a more penetrating analysis of the psychology of orientation in space. Such an analysis should presumably be based on a *continuous* examination of the patient's response to the same question—continuity being obtained repeating the same question every minute. Simultaneously a variation of the experimental conditions should be attempted as regards the factors which beforehand must be considered relevant. One group of patients may e.g. be given the possibility of visual orientation while in another the response may be recorded when the patient's eyes are covered after the shock. A comparison may also be made between the response of a patient who has stayed a few days in hospital and of patients who have spent several weeks in the department—in order to attempt an elucidation of the significance, if any, of the opportunity the surroundings have had of impressing themselves on the patient. Parallel to the questions as regards orientation in space the patients may—likewise through a continuous questioning—be subjected to one—or at most a few—simple tests, e.g. with a view to perception or memory. It is obvious that such a procedure would require a very large material. It would, however, be quite possible to procure such a material, and through such an investigation certain experiences might no doubt be accumulated which would give us a more thorough knowledge of the psychopathology of the orientation in space.

The above remarks with regard to orientation in space as well as to the experimental possibilities within this field will also apply in principle to the category *orientation in time*. The graphs 6-9 illustrate the results obtained by means of the usual question as to year, month, day of the week, and duration of stay in hospital.

It will at once be seen that within this field the performances are considerably inferior to those concerning personal

data. 10 min. after the shock only 2 per cent. of the patients with convulsions are able to give a correct answer to the question as to the year, while none of them are able, at this time, to give a correct reply to the question as to the month, day of the week, or duration of stay. With regard to the patients with petit mal seizures the results are somewhat better, as in this case 52 per cent. of the patients are able to give the correct year already 10 min. after the shock, while the figures with regard to the other three questions are 18, 4, and 9 per cent., respectively. In this connection a gradual increase in the number of correct answers is likewise observed in the course of the subsequent hours. But even two hours after the shock only about 40 per cent. of all the patients are able to state the day of the week and the duration of the stay correctly (figs. 8 and 9), while well over 80 per cent. of the patients at this time are able to state the year correctly.

If with these concrete experiences as a starting point we want to obtain a more differentiated analysis of the concept: orientation in time, it is necessary to form an idea of the psychological "qualities" which is covered by this comprehensive term.

If a patient to the question: "What year is this?" replies "1916", it *may* mean that he actually believes to be living during the first great war, i.e. a real displacement of the orientation in time such as is often experienced in dreams. Usually, however, the reply will only mean that he has no idea whatever of the time. Having—at any rate formally—understood the meaning of the question, he answers "1916" on account of not directly understandable psychological motives. The reply may also cover the fact that he actually has a correct orientation in time, but is unable to mobilize the correct designation of the concept. In such cases, when the apparent disorientation in time is due to a failing ability to mobilize a verbal concept, the reply will, however, more frequently—instead of the correct 1948—be 1946 or the like, which is an expression of a failing retention of the correct designation.

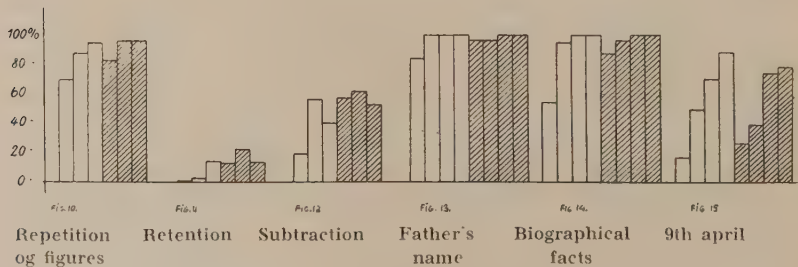
The questions: "What year is this?—What month and date

or day of the week is this?" aim at an evaluation of the so-called *static orientation in time*, i.e. the patient's momentary appreciation of his time relations.

This "static orientation in time", however, merely represents one single "quality" within the field of the consciousness concerned with the concept of time, but a routine evaluation of patients with impaired consciousness will often be aimed merely at an elucidation of this quality. Other elements of a more fundamental nature than this complex and mediate psychic performance that may be mentioned, are: *chronognosia*, *chronometry*, and the experience of *chronology*.

Chronognosia denotes the immediate experience of the duration and course of time and of the temporal continuity of the ego, while *chronometry* refers to the relation between the immediate experience of the rate at which the events follow one another and the actually measured time. The former experience thus has a retrospective object, the latter has for its object something which is momentarily taking place. *Chronology* finally refers to the sequence of events.

It is outside the scope of this paper to discuss the methods which may be applied for the evaluation of these elements of the consciousness. Such an evaluation is fundamentally possible, and if the results were considered in conjunction with the results of a simultaneous analysis of other integrating elements of the consciousness, it would be possible to some extent to elucidate the normal psychology of the experience of time or temporal orientation.



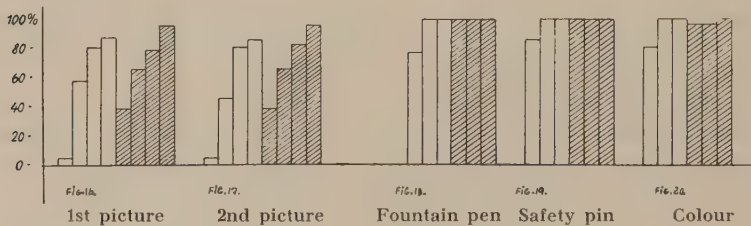
Figs. 10-15 illustrate the results of the preliminary *reten-*

tion tests and *memory tests* which have been used for these investigations. When considering the significance of these graphs, it should be remembered—and this applies particularly to the first group of tests, i.e. 10 min. after the shock—that several minutes have already passed since the patient was asked the first questions, namely the allopsychic orientation tests. Hence it is not possible to make any comparison between the results of the initial and subsequent orientation tests. During the following groups of tests, i.e. 30 min., 60 min., and 120 min. after the shock, the time interval has been diminished because the examination as a whole now takes up less time. Further the variation in the lucidity of the consciousness from minute to minute is smaller than immediately after the shock. It must therefore be considered warrantable with regard to the 2nd, 3rd, and 4th group of tests to compare the results of the tests within each group.

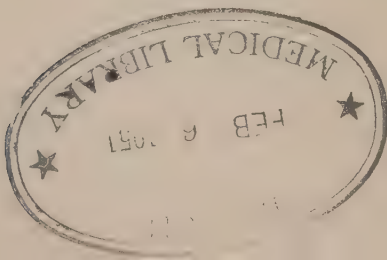
It should, however, be added that an evaluation of the power of retention as well as the content of the memory in patients with impaired consciousness is on the whole a dubious matter. The result of the test is perhaps to a greater extent dependent on the question whether the task is understood by the patient and on his power to concentrate on a given task than on the condition of the relevant psychic functions, i.e. the power of retention and ability to mobilize remembered facts.

For these reasons we shall refrain from discussing our preliminary results in this field. It is, however, of interest to note that the *power of retention*, expressed in the ability of the patient to repeat memorized figures, seems to *be particularly deteriorated in these patients* (fig. 11). Even one hour after the shock only 14 per cent. of the patients with convulsions and 22 per cent. of the patients with minor seizures are able to perform this test. At this time all the patients are able to solve *Bourdon's* crossing-out test correctly. The picture-description test is also performed with a positive result in this third group of tests by more than 90 per cent. of the patients. The patients are thus at this time quite able to comprehend

a complicated task, to concentrate their attention on it for a certain time, and to mobilize the designations of a number of complicated concepts. The result of *Ranschburg's* retention test two hours after the shock also indicates that the power of retaining memorized matter is particularly highly compromised in these patients. Two hours after the shock 60 per cent. of the patients are unable to repeat more than 4 out of 9 word-pairs immediately after memorizing them, and only about 10 per cent. are able to retain more than 6 word-pairs. There is hardly any doubt that these figures represent a rather highly compromised power of retention for the time after the shock.



In conjunction with tests as to the content of memory and power of retention we have endeavoured to throw light upon a possible *retrograde amnesia*. As appears from figs. 16 and 17 this part of the investigations has to some extent given a surprising result. The test consisted in showing the patient 7 pictures from a picture-lotto and asking him to pick out 2 pictures which had been shown to him 60 min. and 5 min., respectively, before the shock. A priori, amnesia for the picture shown 5 min. before the shock might have been expected to be more frequent than for the other picture. However, this was not found to be the case. The course of the graphs representing the correct replies to this test are identical for picture 1 and picture 2. It is thus seen that 30 min. after the shock there is amnesia for the pictures shown in 40 per cent. of the cases—both as regards picture 1 and picture 2—and that 120 min. after the shock this figure has been reduced to 10 per cent.



If it is at all allowable to draw comprehensive conclusions from these preliminary results as regards the retrograde amnesia, the following may be stated: at any time after the shock a retrograde amnesia may be ascertained in a certain number of patients. In so far as it is possible to ascertain any amnesia, it seems in the major part of the cases to cover more than one hour. The amnesia disappears in the course of the first few hours after the shock. This does not occur as a gradual reduction of the extension of the amnesia, but the fairly extensive retrograde amnesia (> 1 hour) suddenly vanishes and the memory of events immediately preceding the shock is re-established.

It is superfluous to emphasize that the slight material presented here does not in any way permit a formulation of concrete conclusions of final validity with regard to the phenomena observed. Neither has it been the aim of the investigators to form such conclusions. As regards the particular psychological mechanism of the retrograde amnesia the problem is in itself so highly differentiated, and the secondary psychological factors are so numerous that a final interpretation of the results will require a very considerable material and a planning in detail of the course of the investigations. It would—if the technique applied to the present investigations were to be used—be necessary to vary the interval elapsing between the initial memorizing of the different objects. It should also be endeavoured to vary the nature of the event or experience before the shock which is intended to be used as a test object for a retrograde amnesia. The patient may here either be faced with visual or auditory stimuli; with events of quite an abstract nature without any actual conceptional content or with “ready-formed” impressions; with purely neutral experiences, or experiences of a certain affective content, etc., etc.

The *ability to name objects* represents a simple and moreover fairly illustrative apperception test which simultaneously illustrates the patient's visual apperception and his ability to mobilize the verbal designation of an experienced concept.

The results of these tests are given in figs. 18-20. It appears from these graphs that the perfectibility of the patients—at any rate as regards the designation of fairly elementary objects—is fully reestablished already within 30 min. after the shock. We have committed the technical error of placing these tests too late in each group of tests. As already mentioned this fact has a certain influence, particularly on the first group of tests, i.e. 10 min. after the shock, at which point the interval between the initial and final test is still fairly long. For this reason the results of these tests in the first group of tests are too favourable and cannot be compared e.g. to the allopsychic orientation tests.

It has previously been emphasized that while evolving the procedure for these preliminary investigations we have not distinguished between the “impressive” and the “expressive” elements of the psyche. The major part of the tests used have, as will already have appeared, been “mixed”, in so far as the patient’s response is conditioned by a perception of external stimuli as well as expressive action. It has likewise been emphasized previously that we consider this to be a fundamental weakness in the planning of the work, and we are of the opinion that a revision of the method should primarily be aimed at this problem.

If, however, the aim is thus to plan a technique on the basis of a distinction between special “elements” of the consciousness, the formulation of the problem should be based on a clear realisation of the fact that the ideal requirement to all research work: a purely objective recording of the phenomena, is in this case fundamentally illusory. The manner in which the problem is approached, i.e. the choice of observation *method* and the concepts applied to the description of the observations, is in itself a factor which will have an essential influence on the results.

As regards *apperception* it will be seen that an evaluation of this “quality” may be based either on the concepts of the classical atomistic psychology or on a “global psychological” description of the phenomena.

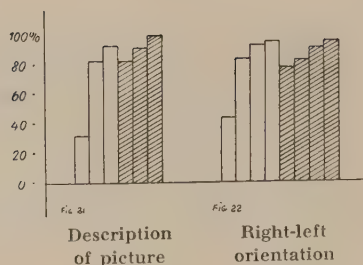
In the first case apperception will be defined as a sensory phenomenon (a perception), accompanied by or associated with a conception of the nature of the object of the sensation, and the analysis of the patient's response will have to aim at a distinction between "purely sensory elements" and "ideal data" or conceptional elements in the patient's experiences—and the investigations will have to be planned in such a way that such a distinction is rendered practically possible.

From a "global-psychological" point of view the evaluation of the *same* elements should aim at a demonstration of a possible alteration in the patient's total experience when faced with a complex of external influences, i.e. the investigations will have to be planned with a view to a description of the "Gestalt-function" of the patient. It is evident that a final evaluation of the patient's "apperception" will differ formally according to the question whether the "analyzing" or "globalizing" method has been used.

Before deciding which method is to be used, it is useful to obtain a clear idea of this fundamental relativity of the concepts, even if the considerations may perhaps appear somewhat general and theoretical. They may have the practical consequence that they justify a further differentiation of the investigation technique. If it is thus determined to base the investigations on an evaluation of "impressive" and "expressive" phenomena of the consciousness, respectively, this distinction will in itself express an "element-psychological" conception of the phenomena of the consciousness which—as a necessary supplement—requires a parallel evaluation of the "Gestalt-function".

To return to the apperception-tests applied for the purpose of the present investigations, the *picture-description tests* (fig. 21) show that 30 min. after the shock 85 per cent. of all patients are able to perceive and describe a number of details in a naturalistic picture shown to them or perceive and express the point of the event illustrated by the picture.

The importance of this result is to be found in the fact that it makes it possible to exclude disturbances of appercep-



tion as a reason for negative results of the simultaneous "specific" tests for orientation, retention, memory, etc.

The tests used are, however, quite insufficient for an elucidation of apperception in itself as well as of the gradual reestablishment of this element of the consciousness during the time after the shock. For this purpose it would in the first place be necessary to observe the patient *continuously*, i.e. try to describe the way in which he experiences the various stimuli to which he is subjected at intervals of a few minutes right from the postcomatose state of sopor until his consciousness is again perfectly clear.

Secondly it will be necessary to vary the nature of the sensory stimuli to which the patient is subjected, i.e. both tactile-algetic, acoustic, and optic stimuli must be used. Especially as regards the latter sensory phenomena we must distinguish between abstract stimuli, not connected with conceptions of any kinds, and stimuli with a well-defined conceptional content—and as to the last-mentioned stimuli it further holds that we must distinguish between verbalized and non-verbalized tests. The investigations should finally be planned in such a manner that it would be possible to describe the patient's experience *solely on the basis of his behaviour*. Even if a non-verbalized performance on the part of the patient only represents an indirect impression of his experience or perception of the stimulus, it may be assumed to differ fundamentally from the reaction which requires a verbal expression, the latter representing a more highly differentiated and consequently more vulnerable "function" than the non-verbalized performance.

CONCLUSION

In what precedes we have already to a certain extent commented on the results of the investigations and in this connection suggested some points on which the method used has proved insufficient. We shall therefore conclude by merely summarizing the experience gained. For this purpose it would be convenient first to account for the concrete results of the investigations and then to draw the lines suggested by the preliminary findings along which the work might be continued.

The concrete results of the investigations have been as follows:

(1) The postcomatose impairment of consciousness is during the first 10 min. after the shock deeper in cases where convulsions have occurred than in cases where the shock has produced loss of consciousness without eclamptic phenomena (petit mal seizures). This difference vanishes in the course of the following 30 min. and cannot be ascertained 60 min. after the shock. On the other hand it has not been possible to ascertain any connection between the dosage and the degree of postcomatose somnolence.

(2) Within the field "*personal data*", name and marital state shows the greatest resistance towards the general impairment of consciousness after the shock, while especially the concept of age seems very vulnerable. 10 min. after the shock about 90 per cent. of all the patients are thus able to give name and marital state correctly while only 10 per cent. at this time is able to state their age. As late as two hours after the shock about 20 per cent. of all the patients are confused as regards their age.

(3) *Orientation in space* is reestablished gradually in the course of the first two hours after the shock and is completely normal two hours after the shock. Compared to this *orientation in time* seems much more vulnerable. As late as two hours after the shock more than 50 per cent. of the patients are thus unable to state the duration of their stay in hospital.

(4) *The power of retention* seems to be highly compromised during the hours subsequent to the shock. As late as one hour after the shock only 15 per cent. of the patients are able to retain figures with four digits after distraction of the attention. On the other hand the power to *mobilize previously memorized matter* seems only to be slightly reduced.

(5) A *retrograde amnesia*—measured by the ability to recognize pictures shown to the patient immediately before the shock—is observed in 50 per cent. of the patients 30 min. after the shock. It disappears in the course of the following hours. However, the period covered by the amnesia does not seem to diminish gradually; the reestablishment of memory is apparently sudden and total.

(6) *Apperception* is a constituent part of all the performances on the basis of which it is attempted to elucidate the above mentioned “specific” psychic elements. Besides these tests the patient’s apperception is evaluated on the basis of his ability to describe pictures shown to him and to name colours and objects shown to him. 30 min. after the shock about 85 per cent. of the patients are able to give a satisfactory description of the content of the picture, while at the same time expressing a comprehension of the point of the picture. It appears from this that negative results of simultaneous “specific” tests are not due to disturbances of apperception.

It is possible on the basis of the above experiences to draw the following general conclusions:

(1) The postcomatose somnolent state after an electric shock is a suitable object for an analysis of the psychopathology of the impairment of consciousness:

(a) because it is possible to obtain a detailed knowledge of the psychic structure of the individual before the manifestation of the pathological condition which is to be analyzed;

(b) because the rapid reestablishment of the consciousness allows for a *continuous* recording of the psychic elements involved;

(c) because it is possible in practice to produce a considerable material, and

(d) because the method allows for repeated analyses of the same patient, which makes it possible to distinguish between "idionomic" and "eidonomic" reactions.

(2) For the purpose of analyzing the elements of the consciousness during the postcomatose somnolent state two methods may be used: It is possible to perform a "transverse" *periodical* evaluation of a number of psychological elements in the *same* patient at different stages of the gradual reestablishment of the consciousness—with a view to a direct elucidation of the psychological connection between such elements. This is the procedure which has been employed for the present investigations. Or one or a few elements may be followed continuously from the postcomatose sopor until complete reestablishment of the consciousness with a view to an elucidation of all phases. The latter procedure requires a very considerable material—i.e. the number of groups of patients should actually equal the number of elements to be studied. When considering that the intensity of the consciousness—especially during the first period after the shock—alters from minute to minute such a continuous recording will, however, be required in order to obtain knowledge of the elements and psychological mechanisms which must be assumed to be constituent parts of such elements of the consciousness as e.g. orientation in space, orientation in time, etc.

(3) If it is decided to use the latter of the two procedures outlined above, it will, however, be necessary to perform in each case a continuous recording of the patient's response to simple apperception tests. This is necessary, in the first place because a disturbance of apperception in itself compromises the "specific" tests: if the meaning of the task is not understood, the response will give no information as to the condition of the specific function; secondly, because apperception is also a "secondary" element in a great number of performances which we try to elucidate by means of the specific tests (comp. e.g. orientation in space).

For this reason the *first methodical requirement* which an analysis of the psychopathology of the impairment of consciousness must fulfil must be that it contains simple and exhaustive apperception tests. Such tests should be formulated in such a manner that the patient's response may be described on the basis of an "element psychological" as well as a "global" conception of the manner of experiencing.

(4) A description of the individual qualities of the consciousness and their actual state, solely based on the results of the usual orientation tests ("How old are you?"—"Where are you?"—"How long have you been here?", etc.) illustrates the patient's total perfectibility within these fields. But it affords no immediate information as to the elements or mechanisms which make up the total performance. The *second methodical requirement* which an analysis of the psychopathology of the impairment of consciousness must fulfil is that the planning should allow for a description of the individual psychological elements which together make up the "total" performance in question. This should be obtained by varying the experimental conditions (as regards orientation in space by recording the reactions of the patient when he is afforded opportunity to orientate himself by visual perception and when prevented to do so).

(5) When evaluating the patient's response or replies to a number of apperception tests, orientation tests, amnesia tests, etc., regard should be had to the patient's premorbid psychic structure in its broadest sense, his individual experiences, etc., just as a certain attention should be given to the varying emotional effect the test may have on different individuals. The *third methodical requirement* should therefore in the first instance be that the patient has been examined before the shock with a special view to the relevant elements, and secondly, that the material is sufficiently large to make it possible to allow for individual psychological factors.

STUDIES ON THE CEREBRAL CAROTID
SINUS SYNDROME¹
AND THE PHYSIOLOGICAL BASIS OF
CONSCIOUSNESS

BY

ELSE MØLLER and IB OSTENFELD

The literature has brought out relatively few descriptions of thoroughly examined cases of entirely cerebral carotid sinus syndrome, and there still remain some unsolved problems in the pathogenesis and paroxysmal mechanism of this syndrome. So we have found it appropriate to publish the present case, together with some considerations on the pathogenesis and paroxysmal mechanism.

The carotid sinus syndrome manifests itself in attacks arising either without any recognizable cause, on movements of the head, or through other factors causing pressure on the carotid sinus. In any of these cases the attacks may be reproduced by pressure on the right or left carotid sinus, or both of them. There are 3 types of the syndrome, differing in the mechanism of the attacks: Vagal type, depressor type, and cerebral type. In addition, there are mixed forms, made up of 2 or 3 types. In the cerebral type attacks are elicited during which no significant bradycardia or fall in blood pressure may be demonstrated. SLIGHT bradycardia or a SLIGHT fall

¹ Report at the meeting of the Danish Neurological Society on October 30th, 1946.

We are indebted to Professor E. Busch, the Neurosurgical Dept. of the Rigshospital, for his kind assistance and valuable criticism in the course of this work.

in blood pressure may be seen in many cases of the cerebral syndrome that are of no consequence to the appearance of the attacks or to the other symptoms during the attacks, as in these cases the attacks will arise and proceed in the same way even though the slight bradycardia or slight fall in blood pressure are prevented by medication.

Hering (1927) showed that the carotid sinus reflex is elicited by stimulation of the carotid sinus; the afferent part of the reflex arch consists in nerve fibers from the carotid sinus through the intercarotid nerve, from which branches are given off to the glossopharyngeal nerve, the vagus, the sympathetic and, presumably, the hypoglossal nerve, too. Centrally the impulse will reach, among others, the vasomotor center. The efferent part of the reflex arch is made up partly by nervous fibers in the vagus, partly by nerve fibers to various vascular regions, the state of contraction of which is significant to the level of the blood pressure, and partly by unknown paths. Normally the reflex arch keeps at a certain tonus, as has been demonstrated by *Hess* (1930), and to some extent the reflex may be induced in normal subjects, in whom pressure exerted upon the carotid sinus most often produces slight bradycardia and some times a slight fall in blood pressure.

CASE HISTORY

(Record No. 434/46.)

Our patient was a man, aged 37, with a negative family history, without previous nervous periods, not subsolid, but probably somewhat subvalid. In connection herewith he has had occasional *déjà-vu* attacks.

From youth, about every 3 months, he has had attacks of intense unilateral headache, now on the right side, now on the left side, over the eye. The headache usually commenced about noon, and it was not accompanied by nausea, vomiting, scotoma, glimmering or other concomitant phenomena. It was aggravated by exertion. When the carotid sinus syndrome developed, the attacks of headache ceased.

Prior to the development of the carotid sinus syndrome, the patient was in some degree under a mental strain, which, together with his fear of the attacks, made him depressed, restless, nervous, and sleepless.

From the winter 1945-46 he had attacks of varying character. The first attack appeared spontaneously in January 1946. Some attacks involved a sensation of suffocation, other attacks involved unconsciousness or haziness followed by a weeping spell; some attacks involved paresthesias in all 4 extremities or precordial anxiety, apnea, or a sensation of heat.

In the spring of 1946 the attacks gradually assumed the character of a definite type, which soon became the only one. The intervals between the attacks varied from a few hours to several weeks. On account of these attacks the patient was admitted to the Psychiatric Department of the Frederiksberg Hospital, on March 23, 1946, where we repeatedly have had occasion to observe these attacks.

The attacks were ushered in by a state of decreased consciousness, during which his speech became slower, hesitant, until finally he was unable to say anything even though—according to his own statement after the attacks—he had known what he wanted to say, and he had realized the word picture. “My brain stopped working, just as may happen at school examinations, when you know a whole lot but can’t say it.” In one attack he proved able to write the physician’s name. He felt empty of thought and slack, being unable to perform even such a simple calculation as 7×8 . In many of the attacks he had a sensation of the visual impressions becoming more distant and of the ceiling rising. He perceived all that was said to him, and he was able after the attack to give an account of what had been said. He felt helpless but not frightened. The facial expression was distant and blurred, and he kept staring straight ahead.

In the spontaneous attacks the pulse was constantly about 60. The pupils were large—also between the attacks—reacting moderately to light. There were no pallor, sweating, or reflex disturbances. He felt weak all over, even though he was able to stand up and, on request, breathe deeply. He felt a continuous whistling in his head. After a few minutes the patient stopped breathing for a short while, and then he had a short, loud crying spell that ceased rather abruptly at the same time as he resumed a more conscious appearance. A little later he was again able to speak normally, and he claimed that now he was feeling well. Most likely, the sensation of utter helplessness during the attack made him unhappy, but the weeping spell was not directly due to any mental affection, but of an entirely reflex character. In each attack the weeping spell set in as a grimace—an objective phenomenon as far as he was concerned—most often sudden and violent. He strongly resented the weeping spell, but he could not help it.

The attacks would set in both in erect sitting and in a reclining posture. Sometimes they were apparently spontaneous, at others they

Rate of metabolism: 96 and 90.

Laryngoscopy, in June 1946, revealed a very slight degree of internus paresis.

Special Examinations:

1. *Sinus pressure.* Pressure exerted against the right sinus as well as the left produced attacks that in no ways differed from the spontaneous ones. Under these attacks the blood pressure showed a systolic rise of up to 25 mm., a diastolic rise of up to 10 mm. The pulse rate remained constant, about 60.

2. *Ascending of stairs.* This exercise elicited an attack that did not differ from the spontaneous attacks and those provoked by pressure on the sinus. After the attack the systolic pressure was 100 (no measurement under the attack). Often the patient was able to ascend the stairs—even fairly rapidly—without having any attack.

3. *Hyperventilation.* After 12 minutes of hyperventilation an attack was elicited, weaker than most of the spontaneous attacks. The pulse kept unchanged. Only slight variation of the blood pressure: 110/80—120/90—105/80.

4. *Injection of 20 mg. mecodrine intravenously* produced a series of severe attacks—as much as 5 attacks within 2½ hours. Each attack was associated with two rises in blood pressure, a slighter one at the appearance of remoteness, a higher rise at the onset of the crying spell. Between the two rises the blood pressure fell almost to the initial level, likewise between the attacks in the series. Bl. Pr. before the injection: 100/70. Between the attacks: about 105/80-70. Bl. Pr. at the appearance of remoteness: 115 (110-120) mm. systolic. Bl. Pr. at onset of the crying spell: about 130-120/75-90. In the interval between remoteness and crying spell: about 105/80.

5. *Injection of 5 cg. nicotinic acid subcutaneously.* The patient presented two concurrent reactions: the symptoms of his usual attacks, though milder than the spontaneous ones, and the phenomena generally seen after nicotinic acid: flushing to the face and sensation of heat. The specific symptoms commenced as early as a few seconds after the injection, and they were distinct before the flushing from the nicotinic acid commenced, reaching their maximum in 4-5 minutes, i.e. after the nicotine acid-flushing had become distinctly visible. The attack differed from the spontaneous in the absence of a crying spell proper, the eyes becoming merely shiny. After 10-11 min. the patient answered questions rationally, although the flushing still was pronounced. The blood pressure in all essentials seemed to follow the flushing and only in a small measure followed the symptoms specific of the patient. *Under the specific attack* the systolic pressure fell a little—from 110 to 105—while the diastolic pressure rose: from 70 to 80. *The nicotinic acid flushing* was associated with a fall in the systolic pressure to 95; while the flush

was subsiding, the systolic pressure rose again to 110; and then it fell again to 100. After the specific symptoms had subsided, the diastolic pressure fell to 70; during the decrease of the flushing it oscillated between 75 and 80. The patient conveyed the impression that some degree of anxiety concerning the examination, besides the pain reaction to the injection, played some role in the production of the attack, which indeed appeared very soon after the insertion of the needle.

6. *Ophthalmoscopy during attacks* produced by subcutaneous injection of mecodrine and by pressure on the sinus. No change in the retinal vessels was noticed. The ophthalmologist (Dr. C. Edmund) found no abnormality *prior* to the injection; still, he observed something that might be taken to remind of transitory arterial spasms, but the eye ground was periodically a little dim—which might explain it. *During* the attacks no visible changes could be made out. Subsequently, in the Neurosurgical Department of the Rigshospital, to which the patient later was transferred (see below), ophthalmoscopy likewise revealed no changes in the eye ground before or under provoked attacks.

7. *Electro-encephalography before and during an attack*, induced by sinus pressure. Prior to the attack the record showed a slight dysrhythmia anteriorly; there was a superposition of higher frequency of 18-20 Hertz, which became dominant after hyperventilation; no foci. On provocation of an attack, convulsive potentials registered before and after the attack, but not during it (E.E.G. No. 443/46, Dep. of Neurosurgery).

8 months after the onset of illness, a palpable intumescence appeared on the right side of the neck, localized to the trigonum cervicale, at the level of the middle of the sternocleidomastoid, anteriorly to this muscle. We took it to be a tumor in the right carotid sinus region.

On this account—and because medicamental therapy had been of no avail—the patient was transferred to the Neurosurgical Department of the Rigshospital, and in August he was operated on by Professor Eduard Busch.

At the *operation*, a greyish-red, somewhat flattened, tumor (size of large mandarin) was removed. It had pressed the carotid backwards and laterally. Microscopic examination showed it to consist of aberrant thyroid tissue.

During the operation the patient twice came near fainting, but had no difficulty in speaking, and no crying spell. Under these two attacks the systolic pressure fell to 90, the pulse rate to 40. These phenomena yielded to lowering of the head-rest, and they did not resemble the usual cerebral attacks. At another juncture during the operation, however, when a certain part of the operating field was touched, a jerk of the left leg was elicited, identical with the jerks described above which the patient had been liable to under the attacks and also in the intervals.

The jerks under the operation were stronger than those observed previously.

After the operation the patient was feeling well. Three days later, he was transferred back to the Psychiatric Department of the Frederiksberg Hospital.

At first the blood pressure kept at a low level. One week after the operation it was 85/55. Then it rose, and at the discharge of the patient, 11 days after the operation, it was 105/65; on reexamination, 2 months later, it was 125/80. On this occasion, the patient stated that since the operation he had had no spontaneous attacks, although he had been exposed to exertion and excitement. It was still possible, however, by pressure on the carotid sinus to elicit an attack, and this attack was stronger in intensity and more extensive than previously. Pressure on the left sinus (contralateral to the site of the tumor) provoked an attack with dimness of vision in the left half of the visual field and jerks of both legs, stronger on the left side. Pressure on the right sinus provoked a strong convulsive attack with left-sided convulsions and torsion of the trunk to the left. During this attack the masseter reflex was accentuated. The blood pressure rose from 120/90 to 140/100. The pulse was slightly accelerated. The convulsions were most pronounced in the left lower extremity, which for 15-20 minutes after the attack showed lowered muscle power and accentuated patellar reflexes. In the same period, after the attack, the abdominal reflexes were found to be more lively, especially the upper left and middle right ones. After the attack, jerks of the right leg could be elicited by plantar stroking of the right foot and by stroking the abdomen.

On repeated examination, one week later, before any pressure was exerted against the sinus, the abdominal reflexes were found to be lively, especially the upper left; and when the upper left and middle right abdominal reflexes were elicited, jerks appeared in the left leg—just as on plantar stroking of the right foot. Electro-encephalography now showed a suggestion of anterior dysrhythmia and uncertain opposite phases posteriorly to the left. Under a provoked attack, strong counterphases were seen posteriorly to the right (at 3.c.) and strong muscle potentials (E. E. G. No. 563. A. Neurosurgical Department).

On reexamination, 17 months after the operation, the patient stated that he was feeling perfectly well now, working and doing gymnastics without any inconvenience. He had had no spontaneous attacks since the operation, but one night about 15 months after the operation he was awakened by jerking of the left leg. This jerking ceased after a few minutes. At his place of work he had had as much occasion to get annoyed as previously, but now he did not mind. He had unusually much to do, but this did not bother him. He seemed to be calm and natural

in his behaviour, and he looked well. Ordinary physical examination revealed no abnormality. Sedimentation rate 8 mm./1 hr. Pulse rate between 72 and 68. Systolic pressure between 105 and 100. On neurological examination the conditions were found to be unchanged since the preceding examination, the positive findings still remaining as follows: Slight mydriasis. Left upper abdominal reflex more lively than the other abdominal reflexes, after a couple of strokes resulting in jerking of the left leg. The jerks increased on repeated strokes. In most tests, the right patellar reflex was a little more lively than the left one. Plantar stroking of the right foot gave rise to jerking of the left leg, besides the normal plantar reflex on the right side. On plantar stroking of the left foot there were defensive motions, which on continued stroking went on to slight jerking of the left leg, while at the same time a normal plantar reflex was elicited on the left side.

Forced plantar stroking of the right foot produced an attack of jerking, which augmented into tonic flexion-spasms and finally convulsions of the left lower extremity, speech was abolished, and the patient looked a little remote. The jerks lasted for about 5 minutes; after about 10 minutes the patient again spoke normally and was feeling well. The right patellar reflex was more pronounced than the left and jerking of the left leg was still being elicited by abdominal or plantar stroking.

This attack was not associated with any loss of tonus or crying spell, but otherwise it quite resembled the previous attacks. The blood sugar concentration was followed under this attack, but as the patient was not fasting, this might hardly allow of any conclusion; besides, the demonstrated variation in blood sugar was only relatively slight, amounting only to 23 mg.%, while prior to the attack the spontaneous variation amounted to 27 mg.%.

RECAPITULATION OF THE CASE HISTORY AND FINDINGS

Man, aged 37, without any sign of constitutional nervous disposition.

After moderate psychic strain, in the winter 1945-46, the patient had attacks of decreased consciousness and lacking capacity for speech, loss of muscular tonus, tinnitus, sensation of helplessness and, finally, crying spells. The frequency of the attacks lasted from several attacks daily to one weekly attack, or even less frequently. The attacks could be reproduced by pressure on the carotid sinus. Ordinary physical and neurolo-

gical examination showed no abnormality. Eye examination revealed hypermetropia and mydriasis. Ophthalmoscopy gave normal findings. Blood pressure, on admission, 135-100, later 90-125/70-90. Pulse rate 60-72. No orthostatic hypertension.

SPECIAL EXAMINATION

1. Sinus pressure: + attack, like the spontaneous ones. Systolic pressure rising up to 25 mm.

2. Ascending of stairs: + attack, like the spontaneous.

3. Hyperventilation: + attack after 12 min., but weaker than the spontaneous; rise in blood pressure 10 mm., systolic and diastolic.

4. Mecodrine, 20 mg. intravenously: 5 strong attacks within 2½ hours, each attack being associated with two rises in blood pressure.

5. Nicotinic acid: 5 cg. subcutaneously: + weak attack, without crying spell, a few seconds after the injection. After a couple of minutes, flushing to the head and sensation of heat. *Slight* fall in blood pressure under the specific attack, more pronounced under nicotinic acid flushing.

6. Ophthalmoscopy, under provoked attack: No changes in retinal vessels.

7. Electro-encephalography under attack: Convulsive potentials before and after the attack, not during the attack.

FURTHER COURSE

After some months, local symptoms pointed to the carotid sinus region on the right side, and after 8 months an intumescence was palpable in the right side of the neck. On account of this finding, and as medicamental therapy had been of no avail, the patient was transferred to the Neurosurgical Department of the Rigshospital where operation revealed the presence of a tumor (size of a large mandarin), which was removed. This tumor consisted of aberrant thyroid tissue. It had pressed the right carotid artery, posteriorly and laterally. Under the

operation there was twice a tendency to fainting, with fall in blood pressure and pulse rate, but without difficulty in speaking or any crying spell; on the whole, these two attacks under the operation had no resemblance whatever to the usual cerebral attacks.

After the operation the spontaneous attacks subsided, but it was possible by sinus pressure at the following ambulatory reexaminations to elicit attacks, increasing in intensity and extent. In the last month prior to the operation the attacks were associated with jerking of the left leg, but for some months after the operation the attacks were accompanied by convulsions, especially on the left side, and torsion of the trunk to the left. For 15-20 min. after the convulsions there was paresis of the left lower extremity, with increased patellar reflex. Outside the attacks and also in connection with them there were some peculiar reflex disturbances. During the attacks there was dimness of vision in the homolateral half of the visual field. On subsequent ambulatory reexamination, 17 months after the operation, the patient felt perfectly well, being able to work and do gymnastics without any inconvenience. In the intervening period he had had no attacks, but once—15 months after the operation—he was wakened in the night by jerking in the left leg. Physical examination still revealed the abnormal, peculiar reflexes, which were increasing gradually on repetition of their production, resulting finally in jerking in the left leg, gradually augmented into tonic spasms with flexion of knee and hip, and at last resulting in an attack similar to the ones which previously could be elicited by pressure on the carotid sinus, but now there was no crying spell.

Our *diagnosis* is: Cerebral carotid sinus syndrome.

There seems to be no reason to attach any significance as far as the clinical picture is concerned to the fact that the tumor consisted of thyroid tissue. The rate of metabolism was not increased.

COMMENTS

It seems obvious to interpret the cerebral carotid sinus attacks here described as being of a central nature resulting essentially from some obscure dysfunction of a center in the midbrain for vegetative functions. This is suggested by the following two phenomena:

1. The attacks could be provoked from the normal left sinus as well as from the "affected" right sinus. (This indicates a central (cerebral) disturbance, not merely a peripheral disturbance of the right carotid sinus.)

2. The decrease in consciousness during the attacks and the abnormal course of the reaction with *rise* in blood pressure on pressure being exerted upon the sinus. These symptoms appear to point to the region of the hypothalamus, in which there are centers for regulation of the blood pressure as well as centers for regulation of the state of consciousness—as is evident especially from the studies reported by *Hess* and by *Ranson*. In all probability, the following phenomena likewise point to the midbrain:

1. The crying spells. According to *Kleist* (1937), crying spells may be explained as resulting from involvement of the midbrain in various morbid processes. (According to *Kleist*, however, crying spells may be encountered also in thalamic processes.)

And perhaps: 2. The pronounced loss of muscular tonus. According to *Gellhorn* (1943) and *Koch* (1932), the carotid sinus pressure normally influences the somatic nervous system, and thus it may affect the tonus of the striated musculature. How this takes place is still somewhat obscure, but this phenomenon seems most likely to be due to processes in the extrapyramidal system. According to *Biggart* (1944) and others the hypothalamus has connections with the subcortical nuclei as well as with the autonomic nervous system, to which the carotid sinus gives off impulses (cf. *Gellhorn*, 1943, and others). So it is not excluded that the loss of muscular tonus might be due to reflexes from the

autonomic system over the hypothalamus to the striate system. When in our patient the loss of tonus was so pronounced, it may be due to some vegetative disturbance with abnormally strong influence of the autonomic system upon the striate system. This may perhaps be parallel to the changes in muscular tonus seen under emotion. We have to emphasize, however, that we are unable to prove the correctness of this view, and that influence of the carotid sinus upon the somatic nervous system outside the hypothalamus cannot be excluded.

Among kindred conditions, presenting at the same time both vegetative symptoms and alteration of the consciousness, we may mention *Gowers'* vasovagal attack and *Penfield's* autonomic diencephalic epilepsy. In "Epilepsy and Cerebral Localization", *Penfield & Ericksson* (1941, l. c. p. 93-94) mention the tonic "subcortical" attacks in subcortical epilepsy and similar conditions in injuries to the corpus striatum and in epidemic encephalitis; the description of the tonic spasms which in this condition are seen in one or two extremities present some points of resemblance to the jerks of the left leg seen in our patient during and outside the attacks, and also to the convulsions which our patient had at the ambulatory reexaminations.

Kleist (1937) mentions that convulsions may be elicited from the brain stem and perhaps be connected with an altered vegetative-nervous adjustment.

It is only reasonable to imagine that the mentioned central dysfunction is connected with the circumstance that the "affected" right carotid sinus continually gives off abnormal impulses to the center, whereas in normal subjects the sinus continually sends normal impulses through the center—as mentioned, for instance, by *Hess* (1930), who showed that the reflex arch of the carotid sinus continually is in a certain state of tonus. Conceivably these impulses take their course along the aforementioned paths over the intercarotid nerve.

The special conditions observed under the operation showed that our patient *could* have vagal and depressor attacks—but then without any concurrent cerebral attack. In normal sub-

jects, pressure exerted upon a carotid sinus will most often elicit a vagus reaction with slow pulse and sometimes decreased blood pressure, even though exceptions to this rule are encountered. Among 34 patients with cerebral syndrome *Ferris, Capps & Weiss* (1937) found the pulse more rapid under the attacks in 3, unchanged pulse rate in 5, and a slower pulse in 26. The blood pressure rose in 2 of their 34 patients. In our case the blood pressure rose in response to the sinus pressure, while the pulse remained unchanged, which presumably may be interpreted as attributable to reflex vascular constriction in certain peripheral regions.

At the last reexamination, 17 months after the operation, the blood pressure fell a little during the special attack elicited. Perhaps the matter may stand thus: from the carotid sinus nerve fibers are given off to blood pressure-stimulating as well as blood pressure-inhibiting cell groups in the hypothalamus, so that the reaction in the attacks will depend partly on which fibers are stimulated, partly on which cell groups in the hypothalamus have the strongest tonus at the given point of time.

It is in keeping with the findings in normal subjects (*Koch*, 1932) that in our patient the striated musculature relaxed, and a loss of tonus appeared. In our patient the dysfunction does not manifest itself on this point as a qualitatively abnormal reaction, but merely quantitatively in an abnormally strong reaction.

It is not very likely that the attacks—in particular the loss of consciousness—are connected with changes in the blood supply of the brain. For one thing, during his attacks our patient could assume both erect, sitting, and reclining postures without it making any difference in the attacks. Furthermore, our patient presented no evidence of autostatic hypotension, on which account the attacks could not be ascribed to some mechanism of this type. Finally, the alteration of consciousness had the character of electivity, and it appeared to involve merely the superior functions, the lucidity of which was lowered noticeably, whereas the automatic functions could

be performed just as under normal conditions. Besides, under the operation it was noticed that a fall in blood pressure in our patient was not accompanied by a cerebral attack, although it seems rather improbable that such a fall in blood pressure would not bring about any anemia of the brain.

According to *Ferris, Capps & Weiss* (1937) the state of the pial arteries is not decisive of the amount of blood supplied to the vital brain centers in the midbrain, the dysfunction of which—according to our hypothesis—is of significance to the symptoms appearing during the attack. Still, as these authors find that local vascular reactions—perhaps in the pial vessels—may occur as a *concomitant* phenomenon in the cerebral attacks, it might be that such pial vascular reactions perhaps would prove to be of some significance as an explanation of *some* of the symptoms accompanying the attacks. According to *Fog* (1934, 1937) and other authors, a rise in blood pressure is associated just with a diphasic change in the caliber of the pial arteries: first a passive dilatation that may be absent (*e.g.* when the blood pressure rises but slowly), then an active constriction, appearing after 1½-2 minutes. Even though it thus cannot be excluded that pial vascular reactions may be of some, although slight, significance, it still has to be emphasized that a reduction in the caliber of the pial arteries as resulting from the rise in blood pressure during the attack may play some rôle only in a few patients, whereas it must be assumed that changes in the caliber of the pial vessels in a majority of the patients will go in the opposite direction, as in most patients the blood pressure falls when pressure is exerted on the carotid sinus.

The explanation here advanced of the cerebral carotid sinus syndrome is in harmony with the explanation advanced by *Soma Weiss et al.* (Medicine, 1935) on the basis of thorough examination of 32 patients with carotid sinus syndrome, preferably patients with cerebral syndrome. These authors think that the carotid sinus perhaps has a tonic influence upon the centers for regulation of the state of consciousness and that these centers may be activated from the carotid sinus either

by *direct reflexes* or by way of *localized* vascular reactions. According to *Soma Weiss et al.*, the hyperactive carotid sinus reflex is due to dysfunction of some parts of the autonomic nervous system.

Other theories have been advanced by other investigators. Referring to the studies reported by *Harrison & Fink, Camp* (1944) mentions hypoglycemia as the "trigger-mechanism" in the attacks in patients with the cerebral syndrome. In the case of our patient, nothing may be said about the possible influence of this factor. The patient had not noticed whether he got the attacks when he was hungry.

Dalsgaard-Nielsen (1947) mentions that a certain degree of vegetative lability, constitutional or acquired, is a *conditio sine qua non* for the development of a well-characterized carotid sinus syndrome, and in our patient indeed, such a vegetative lability may very well have been present. *Ferris, Capps & Weiss* (1937) state that various reflexes—not only from the carotid sinus, but also from the pharynx, larynx, pleurae, etc.—under abnormal conditions may have influence upon parts of the autonomic nervous system, so that "organic disease may play a greater role in the development of "vegetative neuroses" than generally assumed." The history of our patient might perhaps be taken as an example of such development of a vegetative lability on the basis of an organic lesion (tumor of the neck). In this connection we wish to emphasize that on the whole, we think our patient has not presented any evidence of neurosis or hysteriform reactions, even though we would not venture to exclude the possibility of a hysteriform reaction towards the end of his illness. (*Kleist* (1937) thinks that damage to the midbrain often makes patients more suggestible and gets them to react hysterically.)

Rossier, Dressler & Sinmen (1940) think that inferior centers in the cerebrum may be inhibited by sinus pressure, so that cortical centers have increased activity and elicit epileptic attacks. And *Stevenson* (1939) holds that the impulses from the sinus pass centrally to the medulla and from there "efferently" to the *cortex* by way of the thalamic region, but

this hypothesis has not been substantiated experimentally. We have also at first been inclined to think that the cortex played the significant role but gave up this trend of thought in favour of the hypothesis advanced here, which offers a better explanation of most of the symptoms.

In our patient we meet with a couple of symptoms that appeared relatively late in the course of the lesion, partly after the operation, and which perhaps falls outside the scope of the explanation offered here for the other, more vegetative, symptoms:

1. The hemilateral dimness of vision. This may perhaps be due to an admixture of migraine elements. Previously the patient had been troubled with attacks of a somewhat uncharacteristic hemilateral headache which disappeared when his carotid sinus syndrome developed. But this coincidence may have been accidental. In the literature we have found no connection described between carotid sinus attacks and attacks of migraine other than the connection emphasized by *Dalsgaard-Nielsen* (1947): that persons with a tendency to attacks appear liable to the sinus syndrome. As explanation of the dimness of vision, however, a functional basis cannot be excluded.

In December 1947, one of us (I. O.) observed a similar case. This patient was a man, 28 years old, who had well-defined carotid sinus attacks, which especially broke out on ascending stairs and running, besides attacks of typical migraine, accompanied by nausea and dizziness, together with acute asthenia. Constitutionally he was slightly inferior. The family history included some cases of neurosis and 1 case of psychosis.—Undoubtedly it will prove of great value to investigate a more thorough correlation between the two lesions in a larger patient material.

2. Convulsions of the left leg. These convulsions may not be due to any functional superstructure. During the operation they could be elicited by touching a quite definite part of the operating field, and they could be reproduced again by touching, appearing within less than one second. Under the operation

these jerks were more pronounced than previously observed by the patient. They were produced only on touching the particular spot mentioned, not during the rest of the operation. These conditions indicate that the jerks constitute a characteristic part of the abnormal cerebral carotid reflex in the patient. The jerks gradually developed into convulsions on the left side, and perhaps they are to be looked upon as abortive convulsive seizures. Possibly the development from jerks to convulsions may be due to a functional superstructure, especially as this development chiefly took place after the removal of the tumor. On the other hand, convulsions, more or less complete, constitute a common feature in the carotid sinus syndrome in many patients—as described in the literature. So the convulsions probably are more apt to constitute a part of the cerebral syndrome—and, if so, as mentioned before, may be elicited from the midbrain. The further course of the syndrome after the operation, as a matter of fact, may conceivably be connected with a paving the way in the reflex arch and irradiation in the nervous system under the repeated reexaminations. Further, it is also conceivable that in the first months after the operation some processes have been going on in the scar during the healing of the tissue, through which the right carotid sinus continuously was subject to an abnormal influence.

3. The transitory monoparesis in the left leg with accentuated reflexes as demonstrated at the reexaminations is difficult to explain—unless it be ypsiliform—without assuming that during the attacks something must have been going on in the cerebral cortex of the patient, not only in the midbrain. It is impossible without encephalography to decide whether there might be a cortical focus that was disclosed accidentally in the course of the disease. After consulting Professor Busch, Chief of the Neurosurgical Department of the Rigshospital, we therefore suggested the performance of encephalography (possibly with subsequent arteriography) to the patient, but he refused to submit to this, as he considered himself well after the operation.

The peculiar reflex conditions and the attack on repeated induction of these reflexes may be due to a functional superstructure.

The preponderant limitation of the attacks to one side of the body is not a phenomenon unique to our patient, as similar features have been described, among others, by *Dalsgaard-Nielsen* (1946), who in 9 patients found hemilateral convulsion (with preponderance to the left in 8 of them) and he explained this phenomenon as due to hemispheric dominance. *Weiss, Capps, Ferris & Munroe* (1936) say that when their patients had convulsions, the convulsions usually started in the contralateral extremities. This also applies to our patient, in whom the right sinus was affected and the convulsions were left-sided. In two cases of cerebral carotid sinus syndrome without unconsciousness, *Engel, Romano & McLin* (1944) found contralateral focal neurological signs, besides abnormal waves in the electro-encephalograms from the ipsilateral cortex. In our patient too the neurological findings point towards the ipsilateral right half of the brain (left extremities). *Rossier, Dressler & Simmen* (1940) also found in three of their five patients that the convulsions were localized to the extremities on one side—or, at any rate, they were predominant on one side.

CONCLUSION

In our patient the explanation of the symptoms in his cerebral carotid sinus attacks—decrease in consciousness, loss of muscle tonus, crying spells and convulsions, but no fall in blood pressure or pulse rate—will chiefly be as already mentioned: *dysfunction of a center in the midbrain for vegetative functions*. This center may lie in the hypothalamus. Besides, we have to assume either that the attacks are associated with cortical processes giving rise to monoparesis of the left leg after the attack—possibly that the patient, in addition to his carotid sinus syndrome, is suffering also from a *cortical affection*—or that a *functional superstructure* has been estab.

lished, something which, according to *Kleist* (1937), often happens after damage to the midbrain. In our patient thus a functional superstructure may have been part of the dysfunction of the center in the midbrain.

This explanation, we have to admit, is based in part on a speculative foundation, and many factors are still investigated but partially. So, here we have advanced merely a hypothesis. Our analysis is to be taken as an attempt to enter a little further into the problems concerning the function of the carotid sinus and thus of the autonomic nervous system.

SUMMARY

A man, aged 37, with a past history of good health, has—without any known eliciting cause—attacks of decreased consciousness, with loss of tonus, under which he is unable to speak, tinnitus, a sensation of helplessness, and, finally, crying spells. The frequency of these attacks varies from several attacks daily to one attack a week or less frequently. The patient is hospitalized, and his attacks are found to be reproducible by pressure on the sinus. After some months of illness, symptoms appear that point to a local affection of the right carotid sinus region; after eight months a tumor in the right side of the neck becomes palpable. This tumor is removed operatively, and in microscopy it is found to consist of aberrant thyroid tissue. After the operation, the spontaneous attacks subside, but attacks may still be provoked by pressure on the sinus, and in the following months these attacks, provoked at ambulatory reexaminations, increase in intensity and extent. Some jerking of the left leg—present already in the last months before the operation, both during the attacks and in the intervals—turn into convulsions, chiefly on the left side.

No fall in blood pressure was ascertained during the attacks—on the contrary, the attacks provoked by pressure on the sinus were associated with a minor rise in blood pressure—and there was no bradycardia. Thus the clinical picture

presented by the patient is an entirely cerebral carotid sinus syndrome. Only under the special operative conditions there were twice a fall in blood pressure and slowing of the pulse rate, without symptoms of the cerebral attack.

On the basis of the clinical features and some special examinations with reproduction of the attacks in various ways, a hypothesis is advanced for explanation of the mechanism of the attacks and of the pathogenesis of the lesion. To a large extent, the symptoms may be explained as attributable to dysfunction of a center in the midbrain for vegetative functions. This dysfunction may have developed through the abnormal emission of impulses from the carotid sinus owing to pressure exerted by the tumor in the neck.

Comparison is made with other cases described in the literature and with the explanations of the cerebral carotid sinus syndrome advanced by other authors—in particular, the view suggested by *Soma Weiss et al.*, which is in perfect harmony with our points of view.

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ON LUMBOSACRAL SPINA BIFIDA
WITH ESPECIAL REFERENCE TO
OPERATIVE INDICATION AND
PROGNOSIS

BY

ELISE TRUELSEN

INTRODUCTION

One seldom experiences anything as tragic as having to witness the joy of a couple of parents after pregnancy and parturition are well over turn to grief because their infant proves to be affected with a malformation which one has to tell them is of serious nature. Some of these children—one is sometimes tempted to say fortunately—have other defects which are incompatible with life, but in many cases a surgical intervention in time may save the child's life. Of the latter some can live a completely normal life, whereas others must live on, burdened with defects of various kinds and severity, more or less excluding them from leading a normal life.

When, shortly after the Department of Neurosurgery, Rigshospitalet, was opened, we were forced to consider the question of *spina bifida*, we could not at the time find any reliable guidance for the prognosis in the literature. Therefore, it was decided to set very wide indications for operation for a number of years in order to obtain definite information about the prognosis by following up a series of patients submitted to the same treatment—particularly as the operative mortality proved to be lower than the literature led one to believe. The present paper is the results of this follow-up.

There have been certain difficulties—not only surgical, but

also in the important matter of *classification* and *nomenclature*.

Earlier classifications have more or less been based on *v. Recklinghausen's* classical papers on spina bifida (1866). Experience made since then has added new types and terms to the forms then described. These additions have of course extended our knowledge of the large number of varieties which must be expected of a condition which like spina bifida interrupts a process of development without, however, contributing to elucidate the natural connexion between the ever increasing number of terms included in the nomenclature. Reviewing earlier publications one will find that nearly every author has his own terminology, at least his own classifications and definitions—a fact which makes a collected estimation of the various reports extremely difficult.

The credit for a new classification and nomenclature for the most frequent and therefore in practice most important localization of spina bifida, the lumbosacral variety, belongs to the French surgeon *Jaques Leveuf*, who has reported the results of his extensive investigations in the comprehensive paper “*Etudes sur le spina bifida*” (1937). *Leveuf's* terminology is based on his own clinical observations verified by patho-anatomical examinations, and it is also intimately connected with the indication for operative treatment and the prognosis for the individual varieties of spina bifida. Apparently, his thoughts are always with the general practitioner or the surgeon who, faced with a new-born infant with spina bifida, is the first to have to consider the question whether operation, immediately or after some time's observation, is indicated, or whether the case is to be given up as desolate—and who, in the first place, has to answer the questions asked by a distressed and anxious parent. It is not least in the matter of these items, so important in practice, that *Leveuf's* classification and nomenclature appears to fill a very perceptible gap.

In preparing our material we have therefore tried to follow the classification of *Leveuf*. It has been connected with certain difficulties as this classification has not been employed

in our case records from the outset (1934). Still, we found it possible and warrantable to classify the cases in this manner on the basis of the descriptions, photographs, reports of operations, microscopical examinations, etc., contained in the case records. Using any other nomenclature we could not either have avoided a certain margin of inaccuracy. In spite of the usage of *Leveuf's* nomenclature and anatomical basic principles, we have, however, found it reasonable to maintain *v. Recklinghausen's* terms in all essentials. This is not at variance with *Leveuf's* principles. If only the definitions are strictly adhered to, it appears to us most practical to maintain old-established terms to the extent they still have a meaning.

Out of regard to the anatomical criteria given by *Leveuf*, which also form the basis of the classification used in this paper, his nomenclature and its basis will be outlined in brief:

According to *Leveuf* a spina bifida is a more or less protruding intumescence filled with cerebrospinal fluid; it communicates with the subarachnoid space and is connected with the spinal canal by a pedicle passing through the posterior wall of the canal, involving the arcus posterior and dura.

This definition will probably jar on many ears. In this country the term spina bifida is ordinarily used for incomplete union of the arcus post. vertebræ, whether it is isolated, perhaps in the form of a small fissure without any pathological significance, or complicated as indicated by *Leveuf's* classification with protrusion of the leptomeninges with or without involvement of the spinal cord. For the sake of clarity this paper uses the term spina bifida in *Leveuf's* definition, but states explicitly "osseous spina bifida" when the osseous defect only is referred to. We have preferred not to employ the term "rachischisis" used by some authors, because it is used by others in quite a special sense. Actually the two terms are Latin and Greek for the same original meaning: split spinal column.

Lumbosacral spina bifida is classified by *Leveuf* into 5 well-defined varieties, connected by transitions; these are natural in an inhibition of development which may occur at

various stages. In this paper only a broad outline will be given of the criteria with a view to what is of most interest in clinical practice. As to further details reference should be made to *Leveuf's* original paper.

To the clinician the decisive points are partly the myelodysplasia itself, partly the condition of the integuments.

LEVEUF'S CLASSIFICATION

Leveuf sets up the following 5 groups:

(1) *Spina bifida with naked area medullaris* (Figs. 1 and 2) (sp. bif. avec aire médullaire à nu), in which case the area is exposed in the deficiently closed meninges, as a rule extended like a mat, perhaps split into two halves, the posterior roots departing laterally and the anterior ones medially. At the distal end of the area the neuroglia may collect and form a *conus terminalis* which, however, often remains enclosed in the wall together with the nerves corresponding to the *cauda equina*. On the other hand, the nerves originating from the more proximal parts usually pass freely through the cavity. Around the area there is a more or less marked meningeal sac, sometimes lax and sunken, frequently protruding and tense—containing the intimately connected arachnoid membrane and pia mater, whereas the dura—as in the other forms—does not extend beyond the limits of the bone defect. At birth the naked area is deep red, but the inevitable surface infection will cover it with a yellowish layer of pus within the first days.

(2) *Spina bifida with connective-tissue covered area medullaris* (sp. bif. avec aire médullaire recouverte de tissu fibreux) differs from the

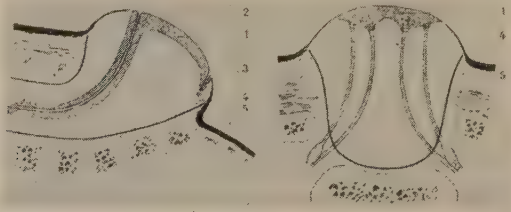


Fig. 1.

Forme avec aire médullaire à nu (after *Leveuf*).

- A gauche: Coupe antéro-postérieure.—1. Aire médullaire.—2. Fossette polaire supérieure.—3. Fossette polaire inférieure.—4. Méninge molle.—5. Dure-mère.
- A droite: Coupe frontale.—1. Aire médullaire. — 4. Méninge molle (zone épithélio-meningée).—5. Dure-mère.



Fig. 2.

NK. 1998. Myelocoele with naked area.

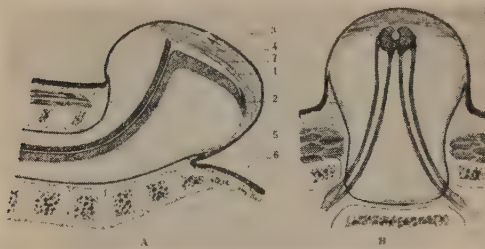


Fig. 3.

Forme avec aire médullaire revêtue de conjonctif d'épiderme
(after Leveuf).

A.—Coupe antéro-postérieure.

1. Aire médullaire longue.
2. Cône terminale.
3. Epiderme.
4. Couche conjonctive susaréale.
5. Méninge molle.
6. Dure-mère.
7. Gouttière médullaire revêtue d'épendyme.

B.—Coupe frontale.

1. Aire médullaire fermée en gouttière avec présence d'épendyme.
3. Epiderme.
4. Couche conjonctive sus-aréale.
5. Méninge molle (zone épithelio-méningée).
6. Dure-mère.
7. Gouttière médullaire revêtue d'épendyme.

previous form only in the respect that at birth the area is covered by a fine layer of connective tissue, only discernible by microscopical examination. This layer is, however, capable of protecting the underlying neuroglia tissue completely against infection. Thus, this variety is not immediately distinguishable clinically from the preceding form, but in favourable circumstances the surrounding epidermis will be able to grow, during the time after birth, from the edge across the area which may acquire a cover of solid integument within 1-3 months.

(3) *Spina bifida with epidermized area* (Figs. 3 and 4) (*formes épidermisées*), where the area medullaris, the spinal cord's place of "insertion" in the wall of the spina bifida sac, is covered with epidermis continuous with that of the surrounding skin, either right from birth or as a later stage of development of a connective-tissue lined area. A characteristic feature of this variety is the great variability in the size of the area, from several centimetres in length to a very small, perhaps terminal fixation of the conus or filum terminale—the form of transition to pure meningocele. Correspondingly, the extent of the myelodysplasia is extremely varying.

(4) *Meningocele* (Figs. 5 and 6) is, in the definition of *Leveuf*, a simple diverticulum of leptomeninges containing cerebrospinal fluid, but not the spinal cord or nerve roots. It may be doubtful whether the transitional form in which the strand-shaped prolongation of the spinal cord, filum terminale, inserts itself in the wall of the sac belongs to



Fig. 4.

NK. 5813. *Myelocoele with epidermized area.*

this or to the preceding form. The fact that the spinal cord and nerve roots remain within the vertebral canal need not mean that there is no myelodysplasia, although it cannot of course be expected to be as pro-



Fig. 5.

Forme sans aire médullaire (ménéngocèle).

(After *Leveuf*).

A.—*Coupe antéro-postérieure.*

- 1. Moelle épinière.
- 3. Epiderme.
- 5. Méninge molle.
- 6. Dure-mère.

B.—*Coupe frontale.*

- 1. Moelle épinière.
- 3. Epiderme.
- 5. Méninge molle (zone épithélio-méningée).
- 6. Dure-mère.



Fig. 6.

NK. 2620. Meningocele.

nounced as in the forms previously described. In the smooth arachnoid lining of the cavity there are often strands resembling nerves. On microscopical examination they, however, generally prove to be strands of connective tissue, in a few cases containing nerve fibres, glia, or even nerve cells—a phenomenon particularly investigated by *Leveuf*, who always found it to be aberrant neuroglia without connexion with the central nervous system—presumably originating from an abnormal foetal displacement and without any practical significance except that it may give occasion to doubt about the diagnosis of meningocele, cf. the definition. The meningocele is always covered with skin from birth, but the integument is often thin and atrophic as in the forms already described, and may be extremely apt to rupture. Unlike the forms described above, its base may be greatly constricted, occasionally forming a thin pedicle in which the fine lumen to the spinal canal may be completely occluded.

(5) *Spina bifida with tumour-covered area medullaris* (Figs. 7 and 8) (sp. bif. avec tumeur) is characterized by the presence of what *Leveuf* calls a tumour, in his experience always a lipoma, between the meningeal cavity and the integument. It is this padding of fat which in this variety constitutes the spina bifida intumescence, whereas the cavity usually does not protrude markedly above the bone fissure. Across the latter there is a layer of fibrous tissue in continuation of the dura. At a place towards the centre this is adherent in the depth and in this

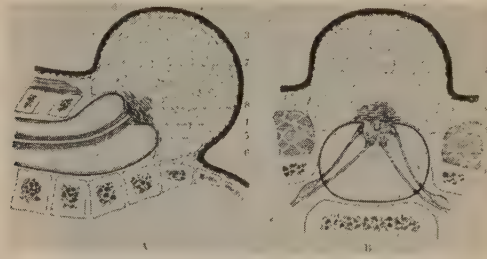


Fig. 7.

Spina bifida avec tumeur (after *Leveuf*).

A.—Coupe antéro-postérieure.

B.—Coupe frontale.

1. Aire médullaire.

1. Aire médullaire.

3. Epiderme.

3. Epiderme.

5. Méninge molle.

5. Méninge molle.

6. Dure-mère.

6. Dure-mère.

7. Lipome.

7. Lipome.

8. Couche fibreuse sus-aréale.

8. Couche fibreuse sus-aréale.

N.B.—Les racines postérieures cheminent souvent en partie dans la paroi du spina, avant de pénétrer dans la cavité.

place there is always a quite small area medullaris, sometimes only a terminal insertion. A peculiarity of this form is the frequent abundance of nervous elements adhering to or enclosed in the wall of the cavity, posterior nerve roots departing from the area medullaris or nerve cords belonging to the cauda equina, whereas these elements in the previously mentioned varieties as a rule run right through the larger cavity without adhering to it. Therefore it is in this variety much more than in the previous ones that an incision of the wall of the sac involves a



Fig. 8.

N.K. 2933. Myelocoele with lipoma-covered area.

considerable risk of damaging the nervous elements. In contradistinction to all the other forms, this variety looks so harmless that in several cases it is not the intumescence as such or immediate striking symptoms of sensory or motor loss that bring the patient to the doctor, but neurological defects appearing later in life.

These are, in broad outlines, *Leveuf's* principles of classification.

WRITER'S CLASSIFICATION

As mentioned above, we have classified our cases by the method of *Leveuf* as far as it has been possible. On account of the fact that our cases have not been observed from the outset with a view to this classification, we have only used 4 of *Leveuf's* 5 groups, namely spina bifida with a naked area, epidermized area, tumour-covered area, and the meningocele. The two last-mentioned groups correspond to *Leveuf's*, whereas the two first-mentioned also include *Leveuf's* "spina bifida with connective-tissue covered area", as this variety

can only be diagnosed by close observation within the first 24 hours of life. Therefore, we have considered the factor of uncertainty too great in our material, as we have only in a few cases seen the patients during the first 24 hours of life, and, if so, only because of urgent indication for immediate operation.

Instead of *Leveuf's* term "spina bifida" which in many minds immediately leads the thoughts on to the defect in the arcus, we have preferred *v. Recklinghausen's* old-established term "myelocoele" for those cases in which the spinal cord is involved in the malformation with an area medullaris and "meningocele" if this is not so. This is not at all at variance with *Leveuf's* definitions which are based on patho-anatomical verification. These definitions have been followed closely, but we have combined them with the simplest of the old-established terms.

Corresponding to the 5 groups set up by *Leveuf* our material of lumbo-sacral spina bifida thus contains 4 groups:

(1) *Myelocoele with naked area medullaris*—comprising this category strictly + the cases in which a connective-tissue covered area may have been impossible to diagnose because of too brief a period of observation—for instance because of operation within the first 24 hours of life.

(2) *Myelocoele with epidermized area*, also comprising this category strictly + the cases with a connective-tissue covered area which during the first weeks of life may become secondarily epidermized. It is known with certainty that several of these cases have acquired their lining of epidermis after birth. Others are not brought to us for operation until so late that it may be difficult to make a distinction on the basis of the appearance and the history.

(3) *Myelocoele with lipoma-covered area*, corresponding exactly to *Leveuf's* tumour-covered area, and

(4) *Meningocele*, corresponding exactly to *Leveuf's* group of the same name.

In addition, we have found it necessary to set up a special group:

(5) *Meningocele with dermoid*. This group does not constitute an absolutely well-defined variety, because in several cases of myelocoele with epidermized or tumour-covered area as well as of simple meningocele small dermoids have been found in the wall, upon microscopical or gross examination, e.g. as large as hazel nuts. These small dermoids are apparently without close relation to anything but the integument,

and they have no connexion with the inside of the cavity, and still less with the spinal cord or nerve roots. In such cases we have considered the finding of the dermoids irrelevant in relation to the myelodysplasia. In a few other cases, however, we have found large, mostly cystic dermoids so closely connected with the meningeal cavity, sometimes even with spinal cord or with nerve roots, that we have considered it necessary to separate them from the smaller ones in a special group. These cases are too few to form the basis of special definitions and too varied to be collected in one. For this reason each case within the group will be dealt with separately.

Eventually, there are within the group of lumbo-sacral spina bifida some cases in which a more or less markedly osseous spina bifida with or without demonstrable meningeal sac, is connected with other malformations of various kinds or with symptoms which do not appear to depend on a myelodysplasia caused by the spina bifida, but would rather appear to represent defects due to arrested development, setting in simultaneously on several points in the foetal organism. These cases are also too different to be collected under one heading, but on the other hand they clearly do not belong to the varieties defined above. Therefore, they also will be dealt with as "special cases".

In collecting this material the writer has perused the case records with great care. In doing so she has repeatedly arrived at a "dead centre", a lacking criterion to prove that it has been this variety or that, but still there has always been some way of approaching a solution, so with a margin of uncertainty, as inevitable as it is warrantably small, the great majority of lumbo-sacral cases have been classified. Others are reported under "special cases". Of course no case has been left out of the material because of difficulties in classification. The purpose of this grouping is primarily to follow the lines indicated in *Leveuf's* paper which appears to us epoch-making, secondly to employ few and simple, but well-defined groups forming a basis for comparison with other materials and especially a basis for a clinical estimation of a future material of patients as regards operative indication and prognosis.

The most important factors in the estimation of each individual case were, apart from the ordinary clinical description, the report of the operation supplemented with an ample collection of photographs made before, during, and after the

operation. Frequently one photograph has contributed more to classify a case than an extremely detailed description. In addition, there have been reports of microscopical examination of removed tissue as well as X-ray films made in nearly all cases. Lastly, these details have always been supplemented with the information obtainable from earlier or later admissions to other hospitals. In nearly all cases we have been given the opportunity to peruse also these case records. Our thanks are due to the hospital departments concerned—mainly pediatric departments in Copenhagen and not least the Orthopedic Hospital, but also to numerous provincial hospitals, hospital physicians and surgeons as well as general practitioners for their great help and kindness, which has often furthered the work decisively.

After the individual cases had been classified in this manner, the patients were called in for after-examination. Considering the extremely difficult situation in Denmark (in the winter 1944-45) one must admire the understanding and interest shown by patients as well as parents in turning up for the after-examination in so large numbers or, if they were unable to come, in answering our enquiries so conscientiously. The follow-up was conducted as an ordinary clinical and special examination as will be seen from the case reports. On account of the lack of X-ray films in Denmark during the war X-ray control could only be made in a few cases where it appeared particularly indicated. In this follow-up study the main stress was laid on forming an opinion of the practical consequences to the patient of any defects revealed by the examination. In other words, whether such defects had only theoretical significance or whether they might, more or less, prevent the patient from leading a normal life or perhaps disable him completely. It is these results and not only the question of merely maintaining the life of the newborn patient that have been intended to form the basis of future operative indications for these anomalies.

It will be seen from the material that the indications for operation have been set extremely wide, and in numerous

cases it appears questionable whether the patients ought to have been operated on. But hitherto it has been difficult to state the prognosis for the individual cases. Little was known about the different varieties and little experience had been gained. It is not until now, when we are in possession of 11 years' fairly unselected material and a corresponding follow-up period, that we have considered ourselves justified in grouping the cases in order thereby to form an opinion of indication for operations in the future.

WRITER'S MATERIAL

Results.

Our material comprises a total of 65 patients, all admitted to Rigshospitalet, Department of Neurosurgery, during the period 1934-45 with a few exceptions, who have been examined and in some cases submitted to operation in other departments and later controlled by us.

Of these 65 patients 43 survived at the time of the after-examination, 17 were dead, and no information could be obtained about the remaining 5.

Of the total number of patients 57 were submitted to operation, 13 of whom have died, 7 in connexion with the operation; 3 could not be traced, so nothing is known of their fate.

Of the patients not operated upon, 4 died, no information could be obtained about 2, and 2 are alive, one of whom has been followed up for 2½ years, the other for 7 months.

The period of observation for the patients now surviving varies from 0 to 11 years. Two have been followed up for more than 10 years, 15 between 10 and 5 years, 20 between 5 and 2 years, 4 between 2 years and 1 year, and 2 below 1 year. Reckoning only with whole follow-up years the average period of observation is 4.6 years.

(1) *Myelocoele with naked area medullaris.*

Our material comprises 3 cases of this group only. This

is not, however, tantamount to this variety being the rarest one. The reason why it constitutes so small a part of our material is no doubt that it is so seldom referred for operation, presumably because of the gravity of the defect which in most cases is evidently irreparable and does not even urge to an intervention in the hope of prolonging the life of the patient.

It was only because of special circumstances that our cases were admitted, e.g. insistent requests from the parents in connexion with the fact that the defects of the newborn infant, like pareses of the extremities, sphincteral insufficiency, etc., could not be diagnosed with certainty at once and a longer period of observation would have meant the most serious risk to the infant's life on account of danger of infection.

Because our cases are so few in relation to the actual frequency of the defect, they are described in more detail than the individual cases of the following varieties.

All three patients were females.

CASE REPORTS

The first patient (1998) had a spina bifida, 4×6 cm., with an area as large as a sixpence. The feet were deformed, assuming a calcaneus position, but otherwise no definite defects, especially no pareses. She was operated on at the age of 8 days without post-operative complications. However, an increasing hydrocephalus developed. She was transferred to another department. At the follow-up the child was found, at the age of 5 years, in an asylum for imbeciles. She presents a tragic sight with an enormous hydrocephalus, the circumference of the skull being 75 cm., about 25 cm. in excess of the measurement normal for the age. She is extremely imbecile, though not quite out of touch with her surroundings, is confined to bed, unable to carry the monstrous head, let alone sit or stand. The deformity of the feet is unchanged, she only moves her legs slightly and is still unable to control bladder and bowel. The scar in the back is solid, but somewhat protruding and distinctly fluctuating. Otherwise she is strongly built and well-developed physically.

The second patient (1547) was also submitted to operation at the age of 8 days for a spina bifida, about the size of a plum, with a small ulcerated area medullaris. The anus is lax, but otherwise there are no definite defects. After the operation she was debilitated, had convulsions,

and microscopical examination of the tissue removed from the sac showed inflammation. Still, she recovered and could be discharged to her home, as yet without other definite defects. At the follow-up, 6 years later, it was impossible to trace the patient and her fate is unknown.

The third patient (H. 43) had an evidently severe myelodysplasia, the spinal cord being spread out like a mat in quite a thin and lax meningeal sac, 8 cm. in diameter. After birth the child was with its mother at a provincial hospital, and as she was still alive, at 3 weeks of age, surprisingly unaffected by the defect, we gave in to the insistent request of the parents and attempted a plastic repair in spite of a beginning hydrocephalus and the evident hopelessness of the case. Primarily the operation appeared to be a success, but post-operatively the hydrocephalus increased rapidly and on the 10th post-operative day the scar became necrotic and perforated; suppuration set in, and the child died at the age of 7 weeks.

In both cases where information was available there was an enormous hydrocephalus which, however, in one of the cases began prior to operation. In the other no hydrocephalus was noted, but the operation was performed at the age of 8 days. One of the children died post-operatively following perforation and infection in the wound, the other is surviving 5 years later, extremely imbecile and totally disabled.

It is unlikely that any patient of this group should be capable of living without operation, and therefore cases that have not been submitted to operation can hardly improve the statistics. The area medullaris is utterly unprotected and inevitably predestined for infection which sooner or later will mean meningitis and death.

(2) *Myelocoele with epidermized area medullaris.*

21 cases:

13 females and 8 males.

17 operated and 4 non-operated cases.

17 operated.

9 died: 4 post-operatively:

2 shocks:

female (3776) operated upon at the age of 3 years, without defects.

female (5297) operated upon at the age of 6 months, sphincteral paresis.

1 meningitis:

female (1208) operated upon at the age of 14 months. No control of bladder and bowel but otherwise without definite neurological defects. No signs of pre-operative perforation of the spina bifida sac.

1 hyperthermia:

male (738) operated upon at the age of 15 months, died during the first 24 hours in a state of hyperthermia. Lacked control of bladder and bowel and was probably slightly deficient mentally.

1 hydrocephalus:

female (2828) operated upon at the age of 4 hours, died at the age of 4 months at another hospital with hydrocephalus. There drainage had been attempted in vain.

1 recurrent pyelonephritis:

male (1673) operated upon at the age of 4 months with signs of slight pareses of the lower limbs, no details as to sphincter function. Died at the age of 14 months.

3 chronic meningitis:

female (1883) operated upon at the age of 1 week, died at the age of 5 months with a severe hydrocephalus, deformity of the feet, massive pareses of the lower limbs and anal paresis. Had pre-operative perforation of the spina bifida sac and the mic. examination of the specimen removed at operation revealed inflammatory infiltration.

female (1884) operated upon at the age of 1 week, died at the age of 2 months. Had total sphincter paresis, pre-operative perforation and inflammatory infiltration.

male (2623) operated upon at the age of 2 weeks, died at the age of 6 weeks with a moderate hydrocephalus and total sphincter paresis. Had pre-operative perforation of the sac.

*7 surviving:**6 poor results:*

female (429) operated upon at the age of 5 months with sphincter incontinence and deformity of the feet. After-examination at the age of 9 years: severe deformity of the feet and massive pareses of the lower limbs, gait very awkward. Complete incontinence for urine and faeces. Lives at a home for invalid children.—Intelligence normal.

male (2007) operated upon at the age of 4½ months with deformity

of the feet and anal paresis. After-examination at the age of 5 years: severe deformity of the feet, gait poor, incontinence for urine and fæces.

female (2132) operated upon at the age of 1 week. Report from another hospital at the age of $4\frac{1}{2}$ years: Gait poor (reflex and sensibility disturbances of the left leg), incontinence for urine and fæces.

male (2141) operated upon at the age of $3\frac{1}{2}$ months with incontinence for urine and spasms in the lower limbs. At the age of 4 we found the patient in a state of deep imbecility in an asylum; no distinct hydrocephalus. He has severe spasms of both lower limbs and considerable hypoplasia of the left and is unable to stand. Incontinence for urine and fæces.

female (3477) operated upon at the age of $2\frac{1}{2}$ months, apparently without defects. After-examination at the age of $2\frac{1}{2}$ years: moderate hydrocephalus and slight intelligence defect, drags the left leg slightly when walking; incontinence for urine.

1 tolerable result:

female (557) operated at the age of 5 months. Report from the mother at the age of $8\frac{1}{2}$ years: Slight hypoplasia of the left leg with some disturbances in gait. Otherwise natural.

1 no information:

male (3730) operated upon at the age of 1 week without definite neurological defects, but with a perforation of the sac. Examined 7 weeks later when he exhibited an increasing hydrocephalus. Two years later it was impossible to trace the patient.

4 not operated upon:

3 died:

male (5813) examined at the age of $4\frac{1}{2}$ months when he had severe deformity of the feet, massive pareses and continuous oozing of urine. Died at the age of 6 months following perforation.

female (N.H.—44) examined at the age of 2 months when she had hydrocephalus, pareses of the lower limbs and continuous oozing of urine. Hydrocephalus increasing. Died at the age of $5\frac{1}{2}$ months following perforation.

female (J.J.—44) examined at the age of 3 months, when she had hydrocephalus, slight deformity of one foot, massive pareses of the lower limbs and incontinence. Died a few days later following perforation.

1 surviving:

poor condition:

female (6514) examined at the age of 3½ months when she exhibited a questionable hydrocephalus, severe deformity of the feet and sphincteral insufficiency. On after-examination at the age of 11 months there was severe hydrocephalus, distinct pareses of the lower limbs and total sphincteral insufficiency. The spina bifida sac was as large as a Jaffa orange and very tense.

(3) *Myelocoele with lipoma-covered area.*

9 cases:

6 females and 3 males.

8 operated and 1 non-operated cases.

8 operated cases:

1 died post-operatively from purulent meningoencephalitis:

Male (3768) operated upon at the age of 7 weeks without definite neurological defects. At operation the lipoma, which on the surface is no larger than a walnut, proves to adhere to the spinal cord by a thick pedicle. When cut this pedicle is seen to contain a dilated central canal. The lipoma continues into the abdomen. Post-operative convulsions, opisthotonos and purulent secretion from the wound. The patient dies 1 month after the operation. Autopsy: Purulent meningitis, pyocephalus int.

6 surviving:

2 poor results:

female (3606) operated upon elsewhere at the age of 13 months for a presumed lipoma in the left buttock. At operation the lipoma proved to be connected with a meningocele, the pedicle of which is then ligated. At this time nothing is stated about sphincter function. At the age of 10 years the patient came to the Rigshospitalet, Department of Neurosurgery, suffering from total incontinence for urine and fæces and constantly recurring pyuria. For these conditions she had been treated in vain during numerous and protracted stays in other hospitals. The anus is lax and open, and there is a constant dribbling of urine. In other respects the child is normal, intelligence natural, and she is extremely unhappy about her condition which among other things prevents her from going to school, so that she has to receive private instruction. Can only be referred to continued symptomatic treatment for pyuria.

male (2933) operated upon at the age of 2 years for a lipoma, as large as an orange, in the sacral region. Incontinence for urine and

fæces. X-ray showed a deformed sacral bone with aplasia of the left pars lat. At operation a lipoma is found to adhere in the depth to a "meningocele". Symptoms remained unchanged after the operation. Report at the age of 5: Incontinence for urine and fæces.

4 tolerable results:

male (1618) operated upon at the age of 25 years. In the sacral region there is a hairy nævus, as large as a shilling. X-ray: Spina bifida of the 5th lumbar vertebra and all sacral vertebræ. At operation a sub-fascial lipoma, as large as a hazel nut, is mobilized and covered with a fascial tent. Symptoms remained unchanged. Follow-up at the age of 31 years: From the age of 16 steadily increasing trophic disturbances of both lower limbs with cold paræsthesiæ, pains and often ulcerations of the feet. Slight difficulty in walking. Both feet submitted to several orthopædic operations, among other things for a growing talipes cavus. Examination shows unilateral absence of Achilles reflex, anæsthesia-analgesia of both feet as well as unilateral riding breech anæsthesia. The patient is capable of working, but is subject to a moderate and increasing handicap. He is married and has 1 child, said to be healthy and normal.

female (1970) operated upon at the age of 25 years for a flat intumescence in the sacral region, as large as half a hen's egg. X-ray: sacral spina bifida. Operation reveals a lipoma adhering to the dura, and when the latter was opened the sacral nerve roots were found to adhere mutually and to the dura. They were mobilized and covered with flaps of fascia. Symptoms remained unchanged and at the follow-up at the age of 30 there was: Varying, slight incontinence for urine; anæsthesia-analgesia in the anal region; states that she is unable to feel urination and defæcation, nor can she feel normal desire to perform these functions. She evacuates the bowel and bladder voluntarily now and then by means of straining. Excision of the presacral nerves at the age of 26 without any effect whatever. She is capable of working, married and has one child, healthy and normal.

female (2505) operated upon at the age of 27 years for a flat, soft protrusion in the sacral region, as large as the palm of a hand. X-ray: sacral spina bifida up to 3½ cm. broad. Operation reveals a large lipoma, part of which is intradural and connected with the spinal cord—which is covered with flaps of fascia after mobilization. Symptoms unchanged and increasing before as well as after the operation. Report at the age of 31 years: From childhood varying, moderate incontinence for urine, increasing trophic disturbances of both lower limbs with tendency to ulceration of

the feet where there is also reduced sensibility. Talipes cavus (orthopædic operations: Tenotomy and cutting of ligaments) and slight difficulty in walking. Uses special foot-wear. Capable of working, but somewhat handicapped. Unmarried.

female (3745) operated upon at the age of 3 years for a pigmented lumbo-sacral intumescence as large as a hen's egg. Her gait is a little awkward. X-ray: spina bifida of the lower lumbar vertebræ, especially of the 5th, and the sacral vertebræ. Operation revealed a lipoma adhering to a small "meningocele", to which the spinal cord adheres; the area is mobilized and a fascial tent made over it. Follow-up at the age of 6 years: Slight disturbance in walking with some spasticity of the right leg, but only slightly handicapped. Perhaps some mental retardation.

1 no information:

female (666) operated upon at the age of 10 months for a flat, soft lumbosacral intumescence. She has a dorso-lumbar kyphosis with a corresponding deformity of the thorax. X-ray shows sacral spina bifida as well as wedge vertebra (with a small rib) between the 7th and 8th thoracic vertebræ; other vertebræ and ribs somewhat crooked and irregular. No neurological defects. Operation reveals a large lipoma adhering to the dura and on the right side going in retroperitoneally. The superficial part of the lipoma is removed. Discharged in good health. Later fate unknown.

1 non-operated case:

Condition tolerable:

female (3714) examined at the age of 7 years with a flat, soft swelling in the lumbosacral region. X-ray: spina bifida of the 4th-5th lumbar and the sacral vertebræ and a malformation with irregular fusion between several lumbar vertebræ. Tendency to involuntary urination when laughing. The right leg is slightly hypoplastic with hypæsthesia of the lateral edge of the foot, where there has also been a tendency to ulcerations for the last couple of years. Right-sided Babinski. Follow-up at the age of 9½ years: Completely unchanged. Carriage and mobility of the back natural; she drags the right leg slightly and wears orthopædic boots.

(4) Meningocele.

22 cases:

11 females and 11 males.

21 operated and 1 non-operated case.

*21 operated cases:**1 dead (no operative death): pneumonia.*

male (1273) operated upon at the age of 6 months for a small meningocele with an occluded pedicle. No defects until he died from pneumonia at the age of 1 year.

*20 surviving:**3 poor results:*

female (612) operated upon at the age of 1 year for a cyst in the sacral region, as large as the head of a child and increasing in size; it reached far into the right buttock, and in the sacral spina bifida, more than 1 cm. in size, the filum terminale and nerve roots could be seen. No signs of neurological defects, especially no sphincter insufficiency. At the follow-up at the age of 9 the child was absolutely normal except for total incontinence for urine. This condition had been treated during numerous admissions to various hospital departments, but in vain. Now only symptomatic treatment of the constant pyuria.

male (2222) operated upon at the age of 1 month for a meningocele as large as a duck's egg. In the depth the nerve roots could be seen following a somewhat irregular course and slightly fixed. They were mobilized. At follow-up at the age of 4 the child proved to be normal except for total incontinence for urine.

male (2334) operated upon at the age of 2 weeks for a large meningocele of typical appearance. No signs of neurological defects. Report at the age of 4 years from another hospital: The right leg slightly hypoplastic with areflexia and diffuse paresis; the left leg is also slightly paretic and the patient is only able to walk in a baby-walker. Total incontinence for urine and faeces. The patient has been recommended to a home for invalid children.

1 tolerable result:

male (88) operated upon at the age of 5 days. Follow-up at the age of 10: The skull slightly hydrocephalic. The appearance of the patient indicates adiposo-genital dystrophy and according to information from his family he is lazy and devoid of initiative. Sphincter condition and lower limbs natural.

16 good results:

female (240) operated upon at the age of 2 months for a meningocele as large as a small hen's egg. Report from the family at the age of 9: Completely natural.

male (430) operated upon at the age of 1 month for a meningocele as large as a hen's egg with a dermoid in the wall, the size of the kernel of a hazel nut. Follow-up at the age of 9 years shows slight hydrocephalus, but natural intelligence; mild talipes cavus and shortening of the left foot; somewhat inhibited dorsal flexion of this foot and absence of the Achilles reflex. Sensibility and sphincteral function natural. The patient uses orthopædic footwear, but moves about completely without restraint; hardly visible dragging of the left leg.

female (352) operated upon at the age of 13 years for a meningocele, the size of a tangerine; it has frequently ulcerated and exuded a clear fluid; she has used a protective cup-shaped leather-bandage. Slight, diffuse paresis and atrophy of the right lower limb. Follow-up at the age of 22 years: Still slight atrophy of the right lower limb with limited dorsal flexion of the foot, hardly visible dragging of the leg. She is not at all handicapped in her work (technical assistant to a dentist) and goes in for games very eagerly.

female (641) operated upon at the age of $2\frac{1}{2}$ years for a meningocele, the size of a walnut. Follow-up at the age of 11 years: Complains of a tendency to cold feet and chafe-sores of the feet, which, however, heal rapidly. Objective examination revealed nothing abnormal.

female (G. R.) operated upon at the age of 1 day for a perforated meningocele. Follow-up at the age of $8\frac{1}{2}$ years: A dysæsthetic spot on the left buttock; otherwise completely natural.

male (535) operated upon at the age of 1 month for a meningocele, as large as a chestnut, which had already been punctured. Follow-up at the age of 8 years: Did not acquire control of bladder and bowel until the age of 4-5, now completely natural in all respects.

female (1699) operated upon at the age of 15 months for a meningocele as large as a hen's egg. Report from the family at the age of $6\frac{1}{2}$ years: completely natural.

male (1889) operated upon at the age of $3\frac{1}{2}$ months for a meningocele as large as a walnut. Report from the family at the age of 5 states that the gait seems slightly peculiar, but the child does not appear to be inhibited and is completely natural in other respects.

female (2341) operated upon at the age of 6 weeks for a meningocele as large as a hen's egg. Report from the family at the age of 4 years: "Nothing abnormal".

female (2494) operated upon at the age of 1 month for a thin-walled, lax meningocele, as large as a shilling. Report from the family at the age of $3\frac{3}{4}$ years: completely natural.

female (2620) operated upon at the age of 3 days for a thin-walled

meningocele somewhat larger than a hen's egg. Follow-up at the age of 3 years: It is stated that she has been rather unwilling to walk and that she was slow in getting control of bladder and bowel; there is still, now and then, nocturnal enuresis. Objective examination reveals a very nervous child (and a nervous mother). She has talipes plano-valgus and wears orthopaedic lifts. Gait good. Lower limbs otherwise natural and there are no signs of incontinence.

male (3191) operated upon at the age of 7 months for a meningocele as large as a hen's egg and slowly growing. Report at the age of 3 years from a provincial hospital where the patient had been admitted for an irrelevant disease: He is said to have walked late and there is still now and then nocturnal enuresis, but otherwise no incontinence. Lower limbs natural and gait good.

male (3836) operated upon at the age of 10 months for a perforated meningocele, the size of a hen's egg. Report at the age of 3½ years from the family doctor: completely natural.

male (5045) operated upon at the age of 1 month for a meningocele as large as a shilling. Follow-up at the age of 15 months: No demonstrable abnormalities, walks normally, no signs of sphincteral insufficiency; is stated to have nearly full control of bladder and bowel. Does not speak yet.

female (5214) operated upon at the age of 7 years for a meningocele as large as a walnut, which previously had been punctured and also had perforated spontaneously. For a period she is stated to have suffered from fainting fits lasting a few minutes, during which she became quite stiff. No neurological defects. Operation reveals the pedicle of the meningocele to be occluded. On follow-up at the age of 8 she complains of tenderness in the back and headache caused by certain gymnastic exercises lying on the back or with the head down. The scar is satisfactory and neurological examination reveals nothing abnormal.

female (5199) operated upon at the age of 2 months for a meningocele as large as a hen's egg. Follow-up at the age of 15 months: Walks, although still in a rather unsteady manner, and has approximate, but not complete control of bladder and bowel. No objective signs of sphincteral insufficiency.

1 non-operated case:

Died of pyelonephritis.

male (2848) examined at the age of 2½ months with an intumescence as large as a small hen's egg, resembling a typical meningocele. Previously fluid had escaped from it, but now it was dry. On admission he was febrile with pyuria and was therefore temporarily

transferred to another department where he died shortly after. Autopsy revealed bilateral pyonephrosis. It is stated that there was almost constant discharge of urine and fæces.

(5) *Meningocele with dermoid.*

5 cases:

2 females and 3 males.

All operated:

1 died post-operatively from collapse following perforation.

female (2216) operated upon at the age of 1 week for a soft lumbosacral intumescence as large as a walnut, which at operation proved to be made up of a dermoid with firmly adherent nerve roots. It is attempted to mobilize these nerve roots, but some of them have to be cut. No definite neurological defects prior to the operation. Post-operative convulsions. Died 11 days after the operation following a large perforation in the scar.

4 surviving:

2 poor results:

male (177) operated upon at the age of 5 days for a multilocular dermoid as large as a tangerine in the sacral region with communication to the spinal canal and with adherent nerve roots. X-ray showed spina bifida. Apparently no pareses or other defects. Follow-up 10 years later showed bilateral pes cavus, poor gait; hypæsthesia on the lateral aspect of the feet and on the medial aspect of the buttocks and thighs. Total incontinence for urine and fæces. The patient has gone through numerous stays in hospitals and in between he has been staying at a home for invalid children. Intelligence normal.

female (492) operated upon at the age of 6 weeks for a multilocular cystic dermoid as large as a hen's egg, communicating with the spinal canal. No neurological defects. A report at the age of 8½ years states that her gait has always been rather poor. She has been submitted to operation for talipes cavovarus and is still under orthopædic treatment. Slight incontinence for urine, mainly at night.

2 good results:

male (2421) operated upon at the age of 2 months for an intumescence the size of a walnut, which proves to be a meningocele con-

nected with a more deeply seated ruptured dermoid to which several nerve roots are fixed; they are mobilized and covered with flaps of fascia. No neurological defects. Report at the age of 4 years states that he is healthy and natural, only he had been slow in learning to walk and therefore has been treated with physical therapy; now he walks normally, but seems somewhat inhibited when running.

male (2467) operated upon at the age of 15 months for a lobulated intumescence, the size of a walnut, of pasty consistency on a broad pedicle. It proves to be a dermoid adhering to the spinal cord. It was partly removed, but during the following year a secreting fistula remains, and therefore a re-operation is made, extirpating a remnant of dermoid as large as a hazel nut. Thereupon the wound heals. At the follow-up examination at the age of 5 years the patient exhibits no neurological defects.

(6) *Special cases:*

5 cases:

2 females and 3 males.

3 operated cases:

2 poor results:

male (2482) operated upon at the age of 45 years. Complaints: From the age of 33 recurrent "sciatic pain", diffuse in the left leg. Obj. exam.: Diffuse, slight atrophy and paresis of the left leg, left equinovarus and absence of left Achilles reflex. When walking he only supports on the lateral edge of the foot. States to be suffering from total left-sided hemihyperæsthesia, most pronounced in the leg. Slight atrophic cutaneous changes on the left leg. Natural motor and static function of the vertebral column apart from direct tenderness of the 5th lumbar vertebra with irradiation to both gluteal regions. X-ray shows spina bifida of the 1st sacral vertebra without definite pathological breadth. Explorative laminectomy shows the fissure to be covered with a firm layer of connective tissue. The film terminale runs through the dura where it is tense, but after opening the latter it can be mobilized. A report at the age of 49 years from the Orthopædic Hospital, where the patient has been controlled states that the complaints and objective condition are unchanged. He does not work and receives an invalid pension.

female (405) operated upon at the age of 43 years. Complaints: From the age of 1 periodic pain from the lumbar column through the left lower limb with increasing difficulty in walking. Obj.

exam. shows a wine-coloured nævus, as large as a half-crown, in the lumbar region, with a fine sinus which is stated to have given off some secretion up to the age of 14, but is now dry. The left lower limb is slightly hypoplastic with hypæsthesia of the medial aspect of the crus. No reflex changes. Walks cautiously and with a slight limp. X-ray shows a severe lumbar scoliosis with rotation and some deformation of the vertebræ; in addition sacral spina bifida. At operation the region surrounding the constriction was excised; beneath this was a fibrous strand to which the filum terminale adhered. Follow-up at the age of 51 years reveals the pain and difficulty in walking to be unchanged, slowly progressing, and, in addition, there is now slight incontinence for urine when the patient is walking. Hypæsthesia and slight paresis of the left leg and absence of left-sided abdominal and lower limb reflexes.

1 good result:

female (2417) operated upon at the age of 35 years. Complaints: Since the age of 10 increasing low back pain, for the last 2 years irradiating through the right lower limb, for 3 months also into the left. Obj. exam. reveals a slight, diffuse reduction of power in the right lower limb. The vertebral column is natural on clinical examination, but there is pain and tenderness over the spinous process of the 5th lumbar vertebra. Absence of right Achilles reflex. X-ray shows spina bifida from the 12th thor. vert.—1st sacral vert. inclusive. Laminectomy of the 5th lumbar vert. reveals the dura to be drawn out into a point adhering to the spina bifida of the 5th lumb. vert; in addition, a connective-tissue strand adheres to this site. The adhesions are detached. The nerve roots looked normal. Report from the patient at the age of 39 years: Quite painless since the operation, but tired in her back. Lower limbs and gait natural. There had been "some transitory difficulty in urination and defæcation".

2 non-operated cases:

No information:

male (5907) examined at the age of 16 years. Complaints: Incontinence for fæces from he was "quite small". The patient is inclined to attribute it to a sacral trauma at the age of 2, but it is impossible to obtain definite information. Urination natural. X-ray has shown lumbo-sacral spina bifida. At the age of 9 a plastic operation on the anus was performed at another hospital without subjective effect. We find the static and motor function of the vertebral column natural. X-ray reveals a broad and yawning defect, occupying the entire sacrum. There is hypæsthesia of the

lateral aspect of the left crus, foot and buttock, otherwise no abnormal neurological symptoms. According to the patient he is unable to feel the desire to defæcate nor the defæcation which occurs involuntarily 2-3 times daily. Rectal exploration reveals quite good power in the sphincter. In view of the extremely uncertain ætiology, the patient was advised to regulate the defæcation to slight constipation, if possible with one firm defæcation daily. Treatment not yet concluded.

male (813) examined at the age of 25 years. Complaints: For the last 2 years uncharacteristic low back pain. Obj. exam. revealed in the lower part of the lumbar region a slightly protruding, fluctuating intumescence with hypertrichosis of the edges and fine telangiectasia. The vert. column was deformed in an S-scoliosis and kypho-lordosis of the thoraco-lumbar region, and X-ray showed spina bifida of the 5th lumbar and 1st sacral vertebræ. No neurological symptoms. Referred to the Orthopædic Hospital, where his pain also is interpreted as being of a static nature, and he is treated with corset. Since then no information.

COMPLICATIONS

Hydrocephalus (Figs. 9 and 10).

The hydrocephalus complicating spina bifida is ordinarily considered to be due to an *Arnold-Chiari* malformation, particularly after *Ingraham's* demonstration of this deformity in 20 cases of myelocele (1944). It has ordinarily been considered the most disastrous complication to spina bifida, either as a primary complication or in some authors' opinion as a consequence of operation with extirpation of the sac. These views seem somewhat exaggerated, and their background must be said to have fallen away after *Ingraham's* investigations.

Penfield & Cone (1932) report 15 cases of lumbo-sacral spina bifida (7 cases of myelomeningocele, 6 of meningocele, 2 of spina bifida occulta with myelomeningocele) upon whom they have operated using a special technique; they preserve the meningeal sac, which is dissected free and covered with a fascial tent after extirpation of the rest—presuming that the ample Pacchionian granulations of the arachnoid membrane play a decisive role in absorbing the cerebrospinal fluid.—In certain cases they also employed slight dehydration and eleva-

tion of the head-end of the bed. They give this technique—probably unjustly—the credit for any of the patients failing to develop hydrocephalus (follow-up period 1 month-8 years).

Francis Grant (1932) reports 6 cases, all of meningocele, submitted to total extirpation of the sac without signs of hydrocephalus after 1 year's observation.



Fig. 9.

NK 1998. Severe hydrocephalus. Myelocoele with naked area.

Gross & Sachs (1934) report 19 cases of spina bifida with a naked area, of whom 17 developed hydrocephalus.

Leveuf's material comprises 2 surviving cases operated upon for spina bifida with a naked area, none of them exhibiting distinct hydrocephalus at the age of $5\frac{1}{2}$ and $2\frac{1}{2}$ years respectively. Among 20 cases of spina bifida with epidermized area observed by the same author 10 operated cases did not develop hydrocephalus, whereas this complication was seen in 5 operated and 5 non-operated cases who died later.

Hindse-Nielsen (1938) has published a large material of patients with cystic spina bifida, comprising myelomeningo-

cele, myelocystocele, pure meningocele and encephalocele. Of these, 52 operated cases were surviving at an age over 50 months, 12 with and 40 without hydrocephalus. In 7 cases the intelligence was below normal, in 45 it was normal. Of 17 non-operated surviving patients—all with a lumbo-sacral



Fig. 10.

*NK 430. Slight hydrocephalus without intelligence defect.
Meningocele.*

spina bifida—none exhibited hydrocephalus; three of them were of inferior and 14 of normal intelligence.

A publication of great importance is the paper by *Ingraham* in 1944, where he reports 20 cases of hydrocephalus in children suffering from myelocele. In all these cases autopsy revealed an *Arnold-Chiari* deformity—i.e. the cerebellar tonsils and the medulla oblongata are drawn down into the foramen magnum by the spinal cord which is fixed to the myelocele. This involves difficulties for the passage of cerebrospinal fluid from the 4th ventricle, and hydrocephalus is the consequence.

After the publication of this paper it can hardly be doubted that hydrocephalus in children affected with spina bifida in

the great majority of cases is due to this malformation and *not* caused secondarily by operation for the myelocoele.

Among our 65 cases 13 exhibited hydrocephalus. They may be grouped as follows:

Myelocoele with naked area:

Two cases out of 3 (no information obtainable in 1). Both cases of hydrocephalus were severe, with an increase in circumference of 25 and 9 cm., respectively (compared with the average measurements of the various age groups stated by *S. Monrad*). The first patient (1998) was 5 years old and extremely imbecile at the last examination; the second (H. 43) died at the age of 7 weeks. Nothing is stated about pre-operative hydrocephalus in the first case, who was submitted to operation at the age of 8 days, whereas the second case appeared slightly hydrocephalic at operation at the age of 3 weeks. The third patient did not exhibit signs of hydrocephalus, either before the operation at the age of 8 days or upon discharge a fortnight later.

Myelocoele with epidermized area:

Of 21 patients 8 were hydrocephalic (9 not hydrocephalic, 4 not known). The 8 cases of hydrocephalus may be grouped as follows:

Three of 9 operated cases, died: 1 severe (+ 18 cm.) died at the age of 5 months, ÷ pre-operative hydrocephalus. No details about intelligence (1883).

Two moderate (+ 5.5 cm.) died at 4 months and 6 weeks, respectively, ÷ pre-operative hydrocephalus. No details about intelligence (2828 and 2623).

Two of 8 operated cases, surviving: Slight to moderate hydrocephalus (+ 4 and + 6 cm.). One operated at 1 week without definite pre-operative hydrocephalus, not seen since discharge at 7 weeks. No details about intelligence (3730). The second one operated upon at 2½ months. At the follow-up examination at the age of 2½ years he appears somewhat backward in intelligence (3477).

Two of 3 not operated cases, died: Slight hydrocephalus (5 cm.), examined at the age of 2 and 3 months, respectively. No details about intelligence (M. H. and J. J.).

One not operated case, surviving: severe hydrocephalus (11 cm.) at follow-up at the age of 11 months. Had a trace of hydrocephalus at the age of 3 months. Intelligence dubious. (6514).

Myelocoele with lipoma-covered area:

9 cases, none with hydrocephalus.

Meningocele:

22 cases amongst whom 3 are hydrocephalic, all mildly (15 non-hydrocephalic, 4 not traceable). All 3 had been operated upon and survived. Hydrocephalus of 4, 5, and 5 cm., respectively. The first patient (88), who was 10 years old at the follow-up, exhibited some mental retardation. His mental state would, however, appear to be ascribable to adiposo-genital dystrophy which probably exists independently of the mild spina bifida. The other two, 9 and 4 years old, respectively, exhibited no intelligence defect (430 and 2334). In none of these three cases there were signs of pre-operative hydrocephalus.

Meningocele with dermoid:

5 cases, no hydrocephalus. All operated.

Special cases:

5 cases, no hydrocephalus.

Our operative technique has been extirpation of the spina bifida sac in toto preserving its meningeal leaf which is sutured beneath the plastic repair (fascia and skin).

Like *Leveuf* we have found no cases of hydrocephalus in the group of myelocele with lipoma-covered area.

The 3 cases of hydrocephalus occurring in our group of meningocele are so mild and so indifferent with regard to intelligence that they cannot be characterized as a handicap to the normal life of the patients. Thus, in accordance with other materials (*Penfield & Cone, Fr. Grant, Leveuf*), we do not find the risk of hydrocephalus to be any contra-indication to operation of meningocele.

The doubtful group is myelocele with epidermized area, in which hydrocephalus occurred in 8 out of 21 cases. The ratio of operated and non-operated cases developing hydrocephalus is 5/17 and 3/4 which does not indicate that the extirpation *per se* promotes the development of hydrocephalus. Hydrocephalus had not been observed prior to the operation in any of the cases, but as a general rule the children are so small at the time that it could hardly have had time to manifest itself. Of the hydrocephalic cases 2 are severe (+ 11.

+ 18) and the one surviving appears to be connected with an intelligence defect. Of the 6 mild cases 4 died before they were old enough to allow of a judgment of their intelligence, the 5th case we have been unable to trace since discharge at the age of 7 weeks, whereas the 6th seems to exhibit some mental retardation. Unlike the group of meningocele this group does not contain any case of slight hydrocephalus which can definitely be said to be without influence on the patient's level of intelligence. On the other hand, we have only one hydrocephalic patient surviving who has reached an age ($2\frac{1}{4}$ years) which allows of a fairly definite judgment as to mental retardation (3477).

Constituting a risk of hydrocephalus of 50 per cent. according to *Leveuf's* material and 39 per cent. according to ours, this factor may be looked upon as a contra-indication to operation. The question is, however, complicated by the fact that it is impossible to base one's decision on the clinical features of the individual, still undeveloped case, but only on the figures afforded by statistics. The demonstration of cranio-lacunae on X-rays of the skull by *Vogt & Wyatt* may perhaps be a help in future. As apparent from what is said below there will, however, in many cases be other factors of greater importance to help one to decide regarding contra-indication to operation.

It ought to be mentioned that in 2 of our cases with hydrocephalus drainage has been attempted in other hospital departments by indwelling catheters inserted through a fontanelle—in both cases without effect. The question as to treatment of the hydrocephalus will be dealt with in another paper from this department.

Sphincteral Incontinence.

Without any doubt incontinence for urine and fæces is the most serious complication to spina bifida.

There are only a few major materials of recent date. In a material of 52 operated surviving patients *Hindse-Nielsen* finds incontinence in

30; of the 22 patients with normal sphincter function 18 had meningoceles and 7 had a spina bifida of a situation higher than the lumbar region.

Leveuf gives the following figures for incontinence in surviving cases above 2 years of age:

Formes ulcérées: 100 per cent. (2 patients).

Formes épidermisées: 78 per cent. (9 of 11, 2 normal).

Formes avec tumeur: 43 per cent. (3 of 7, 4 normal).

Méningocele: 0 per cent. (0 of 7, 7 normal).

Of our 3 patients with *myelocoele with naked area* the survivor, aged 5, was incontinent like an infant according to information from the nurses; she is imbecile, but one must nevertheless reckon with the likelihood of an insufficiency of physical origin. Another patient, whose later fate is unknown, had an obvious anal paresis during the stay in our department. The third died post-operatively at the age of 7 weeks and no information is given of sphincter function.

Of the 21 patients with *myelocoele with epidermized area* 16 exhibited signs of sphincteral incontinence; in 3 cases there are no details, and only 2 were definitely normal. Of these 21 cases 8 were in the age group 9-2¼ years: 6 incontinent (4 for urine and fæces, 1 for urine, 1 stated to be "not continent"); 1 died at the age of 3 years and 1 is surviving at the age of 8 with no signs of incontinence. All had been operated upon.—Of the 13 patients below 2 years 4 had unquestionable incontinence for urine and fæces with constant dribbling discharge (age 11-1½ months), one of them survived at the age of 11 months without operation, 3 died following operation; 3 with constant dribbling of urine and 1 with anal paresis, died without operation; 2 "incontinent" (no further details) died at the age of 14 and 15 months, respectively, both operated upon; in 3 cases no information has been obtainable about sphincter function, one of them being untraceable; the other 2 died, one from pyelitis at the age of 14 months. All 3 had been operated upon.

A comparison of our figures with *Leveuf's* reveals good conformity: 75 per cent. incontinence in the patients above 2 years of age. Calculated on the basis of the entire material 76 per cent. were incontinent and only 10 per cent.—2 of 21 patients—had a definitely natural sphincter function.

Of 9 patients with *myelocoele with lipoma-covered area* 5 were incontinent, 2 of them totally incontinent for urine and fæces (aged 10 and 5 years, respectively) and 3 only with a slight incontinence for urine when laughing, working hard, etc. (aged 30, 31, and 9 years, respectively). The two cases of total incontinence were operated upon at the age of 13 months (in another hospital department and with no details as to previous sphincter function) and 2 years (total incontinence prior to operation). Of the other 3 two were operated upon at the age of 25

and 27 years, respectively; their incontinence remained completely unchanged; the third case, examined at the age of 7 years and again at 9 has not been operated upon.

Of the remaining 4 patients two were surviving at the age of 31 and 6 years, respectively, with natural sphincter function, both operated. One was operated upon at the age of 10 months with apparently natural sphincter function and cannot be traced, and one died following an operation at the age of 2½ months, also with apparently natural sphincter function.

Reckoned on the basis of all the patients sphincteral incontinence occurred in 55 per cent., but disabling in only 22 per cent. Three patients with only slight incontinence for urine are living a normal life, although somewhat embarrassed by the condition: One is a housewife married to a teacher in Copenhagen, the second a maid in a provincial town, and the third an apparently lively and happy school girl.

Of our 22 patients with *meningocele* we are in possession of details about 18 above 2 years of age, all operated upon. Of them 14 are continent; 1 is totally incontinent (4 years old), 2 incontinent for urine (aged 9 and 4 years) and 1 is stated to be "somewhat uncleanly" (aged 3). One of the 14 normal ones is stated to have gained sufficient control of bladder and bowel as late as 4-5 years old. Of the remaining 4 patients below 2 years of age 2, both aged 15 months, are stated to be almost cleanly; one died at the age of 1 year without details being known about sphincter function, whereas one—the only cases not operated upon—died at the age of 3 months from pyelonephritis, with incontinence for urine.

Thus we can reckon with unquestionable incontinence in 3 cases of these 22 patients, i.e. 13 per cent.

The group *meningocele with dermoid* comprises 5 patients. Of them 1, aged 10 years, is completely incontinent for urine and fæces, whereas 1, aged 8½ years, is stated by his doctor to have "some incontinence for urine"; 2, aged 4 and 5 years, have natural sphincter function, whereas 1 died at the age of 19 days without details being known about sphincter function.

Of the rather dissimilar "special cases", all adults, 1 had anal paresis and 1 slight incontinence for urine when walking, whereas 3 had natural sphincter function.

It may seem difficult to decide whether an infant is affected with sphincteral incontinence, and by only a single

examination it may be impossible. Even such an examination may, however, reveal the condition. If the baby e.g. is held up into the vertical position, the urine will, in a case of real incontinence, often be seen to ooze forth and slowly trickle down the legs. Similarly, if one turns the baby in the bed or if it is kicking or crying, one will often see thin masses of faeces dribbling from the anus, although the latter may have failed to reveal definitely abnormal laxness upon exploration. In cases of doubt a brief period of observation will nearly always decide the matter.

In our experience there is no causal therapy for an incontinence due to myelodysplasia. It is only a question of how much help these patients can derive from symptomatic treatment.

Anomalies of the Lower Limbs.

The mobility of spina bifida patients is threatened by various complications in the lower limbs: congenital deformity of the feet, hypoplasia, pareses, disturbances of sensibility, and trophic changes in the skin. We have attempted to collect the material showing the decisive practical importance of one or more of these defects under the collective term *disturbances of gait* in cases where the individuals in question, as in the majority of instances, are above 2 years of age.

Penfield & Cone report 33 cases of whom 7 had pareses of the lower limbs. All 7 belong to the group myelocele or "rachischisis", in their nomenclature the most severe form of myelodysplasia.

Among the 52 operated cases surviving in the material reported by *Hindse-Nielsen* 20 were affected with severe disturbances of motility, 8 with mild and 24 with none. These cases also comprise cervico-thoracic spina bifida. Of 17 non-operated survivors 2 had severe, 8 mild and 7 no disturbances of motility; all 7 were cases of meningocele.

Leveuf has found the following figures for the frequency of club-foot:

Formes ulcérées	41	per cent.	(12 of 29 cases)
„ épiderm.	35	„ „	(9 „ 27 „)
Méningocèles	0	„ „	(0 „ 8 „)
Formes avec tumeur	66	„ „	(6 „ 9 „)

According to *Leveuf* the most common deformity is the severe flatfoot, presumably of paretic origin, the next in



Fig. 11.

NK 198. Severe deformity of the feet. Myelocèle with naked area.

frequency is equinovarus, and finally he finds pes excavatus in only 2 cases, both of "spina bifida avec tumeur."

As to walking *Leveuf* states that none of his 2 surviving patients with *spina bifida with naked area*, aged $5\frac{1}{2}$ and $2\frac{1}{4}$ years, respectively, is able to walk. Of 13 patients operated upon for *spina bifida with epidermized area* only 4 walk normally from the age of 2; 3 aged 4-7 years walk badly, 3 aged 2-4 years cannot walk and 3 aged 10-14 months cannot yet support on their legs. Of 6 operated patients with *meningocele* 5 walk well; still, one of them, aged 13 years, has a hypæsthetic zone on the lateral aspect of one foot with tendency to ulceration, and another, aged $6\frac{1}{2}$ years, has a slight

pes excavatus; the sixth patient was operated upon for an irredressable pes valgus at the age of 18 months and has, in addition, motor disturbances. Of 5 survivors aged 4 to 10 years, operated upon for "*spina bifida avec tumeur*," 1 exhibits marked symptoms of motor loss, 2 are affected with clubfoot and 1 with trophic disturbances.



Fig. 12.

NK. 430. Slight left-sided pes cavus. Meningocele.

In our material the only surviving patient with *myelocele with naked area* has a severe bilateral pes calcaneus and massive pareses; at the age of 5 she is unable to stand on her legs (is also hydrocephalic and imbecile). In the other two cases no details about the lower limbs have been obtainable.

In the group *myelocele with epidermized area* 8 reached an age above 2 years; 5 of them have severe disturbances of gait (2 have pes calcaneus, 1 equinovarus, 2 unilateral hypoplasia of a lower limb; 1 has massive pareses and 2 marked defects

of sensibility); 2 walk tolerably well (one has hypoplasia of the left leg and the other, aged $2\frac{1}{2}$ years, exhibits no distinct special symptoms of motor or sensory loss); 1 walked normally but died following an operation at the age 3. Among the remaining 13 patients who have only been examined below the age of 2, deformities of the feet were observed in 5 (2 pes calcaneus, 2 equinovarus), massive pareses in 6 and signs of disturbances of sensibility in 2. None of this category exhibited trophic skin changes.

Of 8 patients with *myelocoele with lipoma-covered area*, 7 operated upon, 4 walk fairly well (2 have been operated upon for bilateral pes cavus, 1 has a slight right-sided pes cavus and 1 has pes planus; 1 has slight unilateral atrophy and 1 slight unilateral paresis; 3 have distinct zones of hypæsthesia or anæsthesia, all on the lateral aspect of the foot corresponding to the nerve roots L5-S1), 3 walk normally and 1, examined for the last time 10 months old, stood well on the legs, but did not walk yet; in none of the 4 last-mentioned cases could any deformities of the feet or pareses be discovered, but in 2 anæsthetic zones were found. Among these 8 patients 3 had trophic disturbances of the skin, in all cases connected with the typical hyp- or anæsthesia on the lateral aspect of the foot: a male, aged 31 years, who since the age of 26 has been increasingly inconvenienced by callosities and ulcerations of the feet; a female, aged 31, with cool, cyanosed, oedematous and constantly ulcerating skin of the feet and lower part of the crura; lastly a girl, aged 9, who for the last 2-3 years has been suffering from increasing colness, cyanosis and tendency to ulceration of one foot.

Among 18 patients with *meningocele* above 2 years of age, 1 exhibited marked disturbances of gait; it is a boy, aged 4 years, with a unilateral pes calcaneus and massive pareses of both lower limbs. The remaining 17 all walk well; still, 1 of them has a somewhat wadding gait (no local symptoms of motor or sensory loss, but adiposo-genital dystrophy) and 3 drag one leg slightly (a 9-year old boy with a slight unilateral pes cavus, a 22-year old female with a slight right-

sided atrophy of the crus and paresis affecting the dorsal flexion of the foot, and a 3-year old girl without other demonstrable defects than a bilateral planovalgus for which reason she wears orthopædic boots). Without perceptible influence on the gait there is in one case pes planovalgus, otherwise no patient exhibits defects of any kind. Among 4 patients below 2 years of age, one aged 15 months walks well and another, also aged 15 months, walks, though still in a somewhat unsteady manner; about 1 patient, who died at the age of 1 year, it is known that he could stand; the fourth died at the age of 3 months. None of these 4 revealed signs of deformities or pareses of the lower limbs. Thus only 1 of these 21 patients exhibited disturbances of motility of any importance.

In the group of *meningocele with dermoid* there are severe disturbances of gait in 1 (with bilateral pes cavus, hypæsthesia of the lateral aspect of the feet, but no definite localized pareses) and slightly inhibited gait in 2 (one of whom, with a pes cavovarus, has been operated upon, the other without any information about defects); one walks normally and has no defects, whereas one died at the age of 19 days with a paralysis of the lower limbs, not observed until after the operation.

Of the 5 "*special cases*" 2 walk with a slight limp; both have unilateral lower limb atrophy with diffuse paresis, one of them, in addition, pes equinus and hypæsthesia while the other complains of diffuse hypersensibility of the affected leg. The remaining 3 walk normally; one of them has hypæsthesia on the lateral aspect of the left crus and foot. In one patient belonging to this group there was unilateral coolness and atrophic changes of the skin on the crus and foot.

Heredity and Disposition.

Perspectives.

A thorough investigation of matters of heredity in our material of spina bifida falls without the scope of this paper.

Its aim is to find the probable prognosis with a special view to the operative indication for each individual patient, whereas the question of heredity, important as it is, must be solved through other channels. It would require a thorough investigation and personal contact with the family of the patients to the widest possible extent and through several generations as has been done in *Hindse-Nielsen's* fundamental work: "*Spina Bifida Prognose; Erblichkeit*". (1938).

Considering, however, that the factor of heredity is of the utmost interest in connexion with these congenital defects, we have found it natural to try to find out whether similar cases should have occurred in the family by careful questioning of the patients and their relations, usually mothers, with whom we have been in contact during the examination. Our procedure has for instance been to ask a mother about congenital defects, if any, in all her children including stillborn ones, about abortions, if any, about her siblings and their children, her parents and their siblings and in the same manner about the family of her husband as far as she knows, and especially about the occurrence of spina bifida (among the general public usually known as "hole in the back"), club-foot, enuresis, harelip or cleft palate among the members of these families. In addition, a routine questioning—more or less detailed—about hereditary disposition has been made in practically all cases when the history is first obtained on admission. The result has, however, in negative cases been written down as "nothing hereditary" and in positive cases only the individual suspected cases are stated without further information about their siblings.

Therefore, it is evident that the information contained in this paper about familial occurrence of congenital defects does not allow of statistical conclusions regarding heredity or predisposition.—Such conclusions would demand a far larger material. All the same we have thought it right to pass on the information we possess as a modest supplement to earlier and perhaps as hints to future papers on the hereditary aspect of this matter.

In 4 of our 65 cases there is no information at all about familial matters. In 4 cases there is reliable information about other instances of spina bifida in the family; three of them had myelocele with epidermized area and the fourth meningocele.

In the first case (6514) the history contains the passage: "the mother's brother was born with a "water tumour" on his back" and died at the age of 4 months. No further information about the family.

In the second case (1673) information has been obtained about a total of 10 sisters and brothers: The firstborn child is a diabetic; No. 2 is said to have been born "with a deformed head"; then follow 7 healthy children before our patient who is the youngest one and born 14 years after No. 2. Thus, in a family of 10, which probably may increase yet, there are, in addition to a diabetic, 2 cases of congenital malformations. It is further stated that a cousin died with a spina bifida, whereas no information is given about the patient's parents or their siblings.

In the third case (J. J.) the family, which in this as well as in most cases cannot be regarded to be in full yet, consists of 3 girls. Of them both No. 1 and No. 3 had spina bifida and died at 3 days and 3 months, respectively, whereas No. 2 is said to be healthy; both parents are said to be healthy, but no information is given about their siblings or family on the whole.

Our fourth patient (641) had a meningocele. She is No. 2 of a family of 2. No. 1 is healthy and the father and his two siblings are stated to be healthy. The mother's family consists of 4, but with 2 fathers, and a child of the mother's half-sister has a congenital fistula in the cervical region.

Eight other patients have a family history of diseases of a less definite genetic or familial connexion with spina bifida.

In one of these cases (H. 43) the mother is stated to have suffered from salpingitis during her first pregnancy, which was extra-uterine and ruptured; her second pregnancy 3 years later was concluded with the birth of an infant of excessive weight, who died at birth without any further known cause; 2 years later our patient was born with myelocele with naked area and died 7 weeks after an ineffective operation; later the mother has had a child who is stated to be healthy. In the second patient (1208) it is stated that a cousin of the father had rachischisis. In 2 cases (2505 and 3714) a cousin of the patient's is reported to have deformed feet, in the one case more exactly stated as congenital bilateral pes varus. In one case (2141) "a cousin of the maternal grandfather" is said to have 2 imbecile, myxoedematous children. Lastly, one patient's (430) mother's sister at an adult age has been through an operation for a "rudimentary foetus", and 2 patients (2334 and 2848) have a "mentally deranged" mother's sister or brother.

In 2 (3714 and 430) of the last-mentioned 7 patients details are

available about all sisters and brothers of the patient and his parents, in one of them in addition about all cousins on the maternal side. In 2 of the others (2334 and 2848) full details have been obtained about the patient's own sisters and brothers; two other patients (2141 and 1208) are only children and no information is given about the sisters and brothers of their parents. Lastly, there is no information about any sisters or brothers in 1 case (2505).

The remaining 49 patients have no family history of congenital defects according to the information available. As far as 23 of these patients are concerned our only source is the brief "nothing hereditary" from the case records. The majority of these cases have not been followed up because of the patient's early death. Ten of them were stated to be only children, i.e. at any rate first-born children. In the remaining 26 negative cases details are stated about siblings in 9; about siblings and parents in 5; about siblings, parents, and one of the parent's siblings in 2; about the patient's as well as the parents' siblings in 10 cases.

Questions have always been asked about abortions, and, if any, they have been included in the number of siblings. In 3 cases there had been 1 and in one case 4 abortions among the siblings of the patient.

There were no twins among our patients.

Two of our adult patients, a female (1970) and a male (1618) have a normal child each.

In 25 of the 65 cases the patients are first-born children and in merely 6 of these cases do we know that the parents have had other children since. In several of the cases this is, however, probably due to the fact that no contact has been sought with the family later because of the patient's death. Twenty-one patients have a varying number in the family, from No. 2 to 10 in families up to 11. In 19 cases no details are stated about the number in a family, if any.

Nearly always the parents are afraid of having other children with malformations, particularly if the affected child is their first-born. As a rule they can, however, quickly be reassured when they are informed of the small likelihood of a repetition, and then they only long to have the next, presumably normal child as soon as possible. The disappointment appears to be most easily overcome by the parents who either shortly lose a very defective child or by those whose child has been through an operation and then apparently develops normally, although the development is often followed with much anxiety. On the other hand it is so heart-breaking to witness the sufferings of parents who have to watch their

child grow up as a viable individual with defects which cut it completely off from a normal life, that one feels, voluntarily or involuntarily, faced with the problem: Would it not have been better for all concerned, if this child had not lived. Repeatedly a follow-up examination has revealed to us cases in which a child as an infant has been operated upon for its deformation and thus preserved life, but already during childhood disabling defects have placed it outside the company of children of the same age, throwing dark shadows on its own and the family's lives. We remember an example: A couple of middle-aged parents brought their 5-year old son for after-examination. When he was an infant they had been very happy when his life was saved by an operation for spina bifida with epidermized area. It was only gradually that they realized the fate for which he was destined, not so much because of the defective gait and a deformity of the feet which orthopædic treatment at least appeared to help to some extent, but more on account of his total sphincteral incontinence with constantly oozing discharge of urine and uncontrollable defæcation. They love the boy and insist on keeping him at home and taking care of him, and in fact they appear to sacrifice everything for speculations and experiments for the purpose of making his life as "normal" as possible. Without exhibiting any real intelligence defect the boy himself is already nervous and handicapped, probably in part because of constant watching, and in part because of the lack of the company of children of his own age, who of course in no way shut their eyes to his defects. He is excluded from going to school, and finally his father is not to be shaken from his decision not to have more children—"it is enough to sacrifice ourselves for this one." This also deprives him of the company of more tolerant sisters and brothers in the future. And a glance at the despondent, unhappy mother in the background is enough to convince one of the problems and tragedy of this marriage.

Of the severe cases the hydrocephalic children actually appear to be best off. They are removed from their homes in a state of deep imbecility and usually die during childhood.

A slight hydrocephalus does not appear to be a decisive factor. All our cases with up to 5 cm. increase in circumference of the skull compared with the normal measurements for the age, even with a typical hydrocephalic shape, appear to be of normal intelligence, and one does not gain the impression that their appearance strikes themselves or others as particularly abnormal.

Disturbances of gait are more or less handicapping according to their severity. But the very fact that they are accessible to orthopædic treatment is of immense psychological importance and will nearly always open practical possibilities in life, and although the severe cases of this category are disabling, the patients will never be quite isolated from persons of their own age or their equals. There will always be some job and place for them.

The most cruel fate is for the children with incontinence for urine. The constant oozing of urine and the stench from the ever wet pants is an everlasting torment for themselves and their environment. The isolation of these children is complete—children of their own age tease them, they cannot go to school, but must have private instruction, and constant ineffectual treatments and stays in hospitals gradually deprive them of any hope of a cure—they are outside—beyond help, and with a normal intelligence they realize it very early. Some remain in their homes, others are sent to homes for invalid children, where some of them may find their greatest, but poor comfort: that there are others who are in an equally bad or even worse situation.

Lacking control of defæcation is much less disabling than incontinence for urine. Mildly constipating treatment may keep the fæces firm and regulate the defæcation so that there is discharge, e.g., only once every or every other day.

Two of our patients (612 and 5907) have been submitted to plastic operations on the sphincter in other hospital departments without any improvement, and in one case (1970) of mild incontinence for urine we have, by way of experiment, performed resection of the presacral nerves, also without ef-

fect. In the completely incontinent cases we are seriously contemplating closure of the urethra and cystostomy, but we have not tried it yet.

PROGNOSIS AND OPERATIVE INDICATION

Faced with the problem as to whether a child affected with spina bifida is to be operated upon, the surgeon must, in our opinion, try to gain a clear impression of two things: primarily whether the child is affected with defects, malformations, or neurological defects apart from the local spina bifida, and secondarily, for the sake of future prognosis, what category of spina bifida he is dealing with.

A factor of decisive importance to the first item is the possible presence of *hydrocephalus*, the *sphincter function* and the *state of the lower limbs*.

Hydrocephalus is rarely manifest at birth. If a rapidly increasing hydrocephalus, e.g. an increase in circumference of 1-2 cm. a week as we have seen, is demonstrable during the first weeks of life, the prognosis must be considered poor, both with regard to viability and intelligence. Neither *Leveuf's* nor our material indicates that extirpation of the spina bifida sac has any influence on the development of hydrocephalus. Thus, a beginning hydrocephalus will neither speak for earlier performance of an operation, which may have been contemplated for the purpose of improving the prognosis, nor counter-indicate an otherwise desirable period of observation. Similarly, hastening or postponement of the operation for other reasons appears to mean nothing for the development of hydrocephalus.

The factor of greatest importance is the sphincter function, which is of absolutely decisive importance to the prognosis. It is of the utmost importance to try to discern ordinary "infant uncleanness" from actual incontinence, as mentioned in the chapter on sphincteral incontinence, by examining the child carefully when it is kicking, crying or by holding it into the vertical position, etc. In case there is actual incontinence,

the prognosis is poor; an operation for the spina bifida may of course save the child's life, but one cannot hope to save it from disablement. If the infant's condition on the whole allows it, a period of observation, exercising every precaution, is advisable in cases of doubt—it will practically always result in a decision. Finally, one must bear in mind that incontinence for urine is far more disabling than for fæces, which to some extent may be regulated by mildly constipating treatment.

Next in importance is the state of the *lower limbs*, whether they are affected with deformities or pareses. Deformities of the feet are practically always accessible to and often grateful objects for orthopædic treatment, and the patients should be referred to such treatment at an early age. A great deal can also be done about pareses by means of special exercises, splints, plastic repair, etc., but both for the sake of treatment and in order to prevent later disappointment of the parents, one must try to ascertain whether pareses are present, and, if so, estimate their massiveness and extent. A period of observation is often necessary, and at any rate one must exhibit some reservation before declaring that the child is free of pareses. It is very reassuring to watch the newborn infant kicking apparently normally, but it does not exclude the appearance of abnormalities when it has to begin to stand on its legs and walk. On the other hand, pareses presumed to be present at the first examination may prove to be of surprisingly slight significance to the child's gait later, especially under early orthopædic control. But of course it goes without saying that massive and extensive pareses give a poor prognosis, even with special treatment.

Having thus formed an opinion of the child's chances of an approximately normal life, one must—particularly if there are factors of doubt—seek further support in the experience made hitherto regarding the prognosis of the various categories and therefore try to decide which group this particular child belongs to.

As mentioned above we have found *Leveuf's* classification practical, particularly with regard to operative indication

and prognosis. Therefore reference should be made to the introductory description of the various forms.

A *myelocele with naked area medullaris* is usually easy to recognize. During the first 24 hours there is a deep red area, later moist and covered with pus, situated in the centre, or somewhat higher up on the membrane-covered swelling on the back. Faced with this category one must remember that it may be a question of the somewhat milder form in which the area in reality is covered with connective tissue and liable to spontaneous epidermization in favourable conditions. In such cases one must do everything to avoid infection, and *Leveuf* has advocated a method which we have used several times: The baby lies prone in bed with the lower part of the body naked and with an extra mattress or pillow under its stomach, so that the legs are flexed in the hip joint, and urine and fæces flow down the legs; in this way one can avoid irritation and infection of the sac from clothes and especially diapers. The legs have to be protected by smearing them with vaseline and swathing them in cotton-wool and gauze, and an arch across the bed will keep the bed clothes away from the baby's back with the intumescence. Under such conditions one may often see an apparently naked area epidermize in the course of a few weeks.

Myelocele with epidermized area may in turn be confused with *meningocele* or with *myelocele with lipoma-covered area*. It is not always possible to decide with certainty whether the epidermized surface of the sac hides an adherent area medullaris. In case the latter is of any size, one will, however, often be able to palpate it as a firm portion in the fluctuating sac, and as a rule the skin above it will be of an irregular cicatricial aspect. These criteria are not, however, always certain. Actually it may be impossible to decide from an external examination alone whether it is a question of myelocele with a smooth epidermized area or a large meningocele. A method of examination advocated by *Fraser* consisting of roentgenography following injection of oxygen into the cavity is no doubt the most accurate method, but it requires hospitalization. And it

is in these cases of doubt that a period of observation in order to ascertain sphincter function and pareses is necessary to decide the most important question: whether it is desirable that the child be operated upon or not. A small intumescence with a distinctly constricted, perhaps pedunculated base speaks decisively for a meningocele.

A diagnosis of *myelocele with lipoma-covered area* will rarely cause difficulty, if only one keeps the category in mind. As a rule the consistency of the lipoma is easily distinguishable from the distinctly fluctuating and generally more tense character of the previous categories. The lipoma always has a broad base with the peripheral area merging quite evenly with the surrounding subcutaneous tissue, apart from the fact that it is often—characteristically—somewhat pendulous and thus forms a transverse sulcus below the distal part. It may be asymmetrical and for instance proceed into one buttock. As in the previous types, there will often be *nævi* or hypertrichosis in the region, a feature which especially must warn against the assumption of a banal lipoma. A further characteristic feature of this variety is that the surgeon is not presented with the case until the child is a little older. It will, for instance, be brought to the doctor at the age of 4-5 years, because it is unable to walk normally or does not gain control of bladder and bowel, or even later because of the onset of atrophic cutaneous changes or a tendency to ulceration of the feet. The intumescence on the back *per se* may cause so little embarrassment, that no one attaches any pathological importance to it.

A *meningocele with dermoid* may often be difficult to distinguish beforehand from the other forms. The diagnosis is probable when the intumescence is irregular, lobated, and of pasty consistency; but the dermoids are so varied that they may easily cause confusion with all the other forms of spina bifida covered with integument, and only be fully recognized during the operation.

Having formed an opinion of the variety of the spina bifida,

one is left with the consequent prognostic contemplations, but only after an estimation of other defects, if any.

Myelocele with naked area according to our experience has an extremely poor prognosis. Without operation the infant will die. An operation affords a small chance of saving its life, but *Leveuf's* material of 13 and our own of 3 operated cases leave only 3 survivors, all totally disabled, with sphincteral incontinence, pareses of the lower limbs and, in one case, an enormous hydrocephalus.

In case of *myelocele with epidermized area* the prognosis is not materially better. Of 18 operated cases *Leveuf* reports 8 survivors, 2 of whom, however, are completely normal. All the remaining 6 have sphincteral incontinence and disturbances of gait. Our material of 7 survivors among 17 operated cases contains no quite normal and only 1 tolerable result (slight disturbance of gait), but 6 disabled with sphincteral incontinence and more or less severe disturbances of gait. According to the collected material there should therefore be a maximum chance of 8 per cent. for the baby's normal development—a figure which, however, must be taken with every reservation. As stated above, our material is unselected. On account of the risk of perforation and infection, our patients from the first years were often submitted to operation without sufficient pre-operative observation, and several patients have been operated on some months old in spite of sphincteral incontinence and pareses. Employing *Leveuf's* technique of observation the risk of a period of observation is slight, and in case of beginning perforation one may operate immediately, if one wants to do so. If no operation is performed, the patients will, in our experience, always die in connexion with a perforation of the spina bifida sac. But if perforation does not occur during the first weeks of life, one may, even without special precautions, see the babies living and developing for a surprising length of time with the solidly epidermized intumescence which frequently is of a monstrous size. Our material contains cases who have not been operated upon until the age of 6 or 12 months, in spite

of sphincter palsy and then only at the urgent request of the parents. One can imagine the sufferings of a mother who has to watch her baby follow a normal development mentally while the spina bifida sac is growing to a grotesque size. In fact it is no doubt this variety of spina bifida which involves the greatest difficulty as far as the operative indication is concerned. The primary operative mortality is high; without operation the child will sooner or later die from its malformation; and if the child's life is saved by an operation, disablement is more than likely. But one must never overlook the fact that even a child affected with this abnormality may in exceptional cases be neurologically normal, and it is one's duty, as far as possible, to ascertain whether this is so in this particular case.

When we come to *myelocoele with lipoma-covered area*, the problem of indication is very different. There is no risk of perforation, so that the patient's life cannot be considered dependent on operation or not, and, in addition, the operative mortality is low as compared with the other forms. An operation must aim at partly removing the more or less disfiguring visible deformity on the back, partly, if possible, at warding off the trophic disturbances which are apt to be developed by these patients in the course of time. In both respects the indication must depend on the symptoms in each individual case. Actually little is known about the possibility of warding off or improving the trophic late symptoms. One can hope that cautious mobilization of an adherent area or constricting nerve roots may ward off the probable, but not certain development of neurological defects, and *Leveuf* maintains that he has in a few cases seen improvement of symptoms which have already become manifest. In our material we have never seen improvement following operation, and although the stretched nerve roots have been mobilized, trophic disturbances have continued and there has been no possibility of knowing whether the intervention has had any effect one way or another. On the other hand we have once seen some improvement during treatment with vasodilatory medicaments, and in this

case we are contemplating a later sympathectomy, and intervention has been performed in one of *Leveuf's* cases with apparently good effect. One can hardly hope to affect the more serious symptoms like sphincteral disturbances, severe pareses, disturbances of sensibility and reflex—in this as well as in the other categories, they must be considered due to an irreparable myelodysplasia. But seeing that the viability of the patients must be considered independent of operation, their disablement caused by the myelodysplasia is not to be taken into consideration in the same way as in the other categories, when the indications for operation are considered.

The prognosis of *meningocele* is the encouraging factor in the surgical treatment of spina bifida. The operative mortality is unessential—there were no deaths in connexion with *Leveuf's* 7 and our 21 operations for meningocele. On the other hand, operation must be considered necessary to preserve life, at least in cases of large meningoceles, because of the risk of perforation—only the small ones with an occluded pedicle can be considered free of danger. The prognosis is good with regard to mobility. Six of *Leveuf's* 7 patients (of whom, however, one had a meningocele localized to the cervical region) exhibited no abnormalities apart from e.g. a small hypæsthetic zone without practical importance. The 7th patient, a child of 18 months, was treated for a deformity of the feet of doubtful practical significance. Of our 20 survivors—the 21st died 6 months after the operation from pneumonia, as far as we know without defects—17 exhibit similar good results, with only a few cases of slight symptoms without practical importance (a trace of paresis or atrophy without disturbances of gait, minor dysæsthetic zones or a slightly hydrocephalic skull without reduced intelligence). In 3 cases the result is poor—all have incontinence for urine and one, in addition, massive pareses of the lower limbs; one patient is affected with adiposogenital dystrophy, but no symptoms of myelodysplasia. On the basis of the collected material the chance an infant with meningocele has of leading a normal life, following an intervention connected with no more risk than any

other operation, is about 82 per cent, and the chance of disablement about 10 per cent., also calculated on the basis of our unselected material. A number of our patients also in this group were submitted to operation without definite previous knowledge of sphincter function, because of threatening or already manifest perforation. Employing the observation technique of *Leveuf*, one will, however, presumably in these cases, too, be able to wait a few days before operating in order to ascertain symptoms of neurological defects.

As regards the groups *meningocele with dermoid* and *special cases* the indications have to be based on the clinical features of each individual case. At any rate our cases are too varied and too few to justify statistical conclusions.

It will be seen that in practice the most important things are: In the first place to distinguish the cases of meningocele in which operation is necessary to maintain life and the prognosis is good from the other groups with a decidedly much poorer prognosis; in the second place to distinguish myelocele with lipoma-covered area, which does not require operation to be compatible with life and in which the prognosis with regard to disablement is doubtful with as well as without operation. It is in the groups of myelocele with a naked or epidermized area that in many—but not in all!—cases we are faced with one of the most serious ethical problems encountered by a surgeon: Is it right to save a newborn infant from threatening death for an equally threatening isolating, lifelong disablement.

SUMMARY

With application of the nomenclature and classification advocated by *Leveuf*, which is briefly described, a material is reported of 65 patients with lumbo-sacral spina bifida, 57 of whom have been operated upon. A total of 43 survivors have been followed up by reports or after-examinations after a period of observation up to 11 years, averaging about 5 years. Following a short survey of the individual cases, divided into

5 typical groups plus a few atypical cases, the most important complications of the malformation, i.e. hydrocephalus, sphincteral incontinence, and disturbances of gait, are dealt with, each group being taken separately. Comparison is made with *Leveuf's* report of a similar material and a few other reports, and a brief account is given of familial occurrence of the anomaly in a Danish material.

On the basis of this and *Leveuf's* material an effort is made to set up the prognosis for each group, with or without operation, and to state the most important criteria for the clinical distinction between the groups. The importance is stressed of close observation before making a diagnosis and setting the prognosis and operative indication. Furthermore, a description is given of the special technique of observation according to *Leveuf*.

In conclusion, the importance is emphasized of distinguishing between *meningocele*, usually requiring operation to maintain life and having a good prognosis, *myelocele with lipoma-covered area*, not requiring operation to maintain life and where the prognosis is doubtful and not definitely influenced by operation, and finally *myelocele with naked or epidermized area*, which requires operation to maintain life, but—with a few exceptions which ought to be ascertainable during observation—involves a predominant likelihood of life-long disablement.

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ENCEPHALITIS AT BATAVIA

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INTRODUCTION

Encephalitis seems to be a rare disease at Batavia; epidemics are unknown till now, and only a few cases have come under my observation since the beginning of 1931. Records of clinical observations in the central Hospital during the years before the war are not available at the moment. During the two years after the war, at the Neurological Department of the University, where some 500 patients were admitted, half of them Europeans, the others consisting of about 100 Indonesians and 150 Chinese people, not a single case of encephalitis was diagnosed. Furthermore, clinical and postmortem observations during the years from January 1st, 1932, to the end of 1940 in the pediatric ward of the central Hospital are available, as all cases of cerebral disorders occurring there in those years were recorded by me in 1941 (Verhaart 1941). Moreover, the postmortem findings at the Laboratory of Neuropathology at Batavia started in January 1931 are at my disposal. As opening of the skull is a routine procedure in the Pathological Department of the University the number of the brains examined is significant. All together 1,040 brains have been microscopically examined since that time, all of them in cases with some symptom of affection of the brain during life. Of all of them frozen or celloidin coupes or both from parts of the cortex cerebri and of all levels of the brain-stem were stained with hematoxylin and eosin, and when necessary with Hor-

tega's silverstain, with Sudan 3, Spielmeyer, etc. Therefore no case of encephalitis can have escaped attention.

Description of cases:

In the whole pediatric material mentioned above, consisting of 1035 cases of which half were Chinese, 40 per cent. Indonesians and 10 per cent. Europeans, apart from polyomyelitis and a few very doubtful postvaccinal cases without postmortem control, one encephalitis case after measles and three genuine cases were found. In the one after measles, a nine months old Chinese girl, rigidity of the neck, twitchings in the extremities, and conjugate deviation occurred during the day before death. In the brain only one perivascular infiltration with microglia cells and demyelination was found in the cerebral white matter, though a great number of slides were examined.

Of the genuine encephalitis cases the first patient was a Chinese boy 18 months of age, who had convulsions during three days, in his brain the typical changes of v. Economo's encephalitis were found. The second patient was another Chinese boy nine months of age, who will be described later and the third was an Indonesian child six years old, who showed drowsiness, hypersalivation, and strabismus during a few days and subsequently recovered completely.

Cases of encephalitis in the postmortem material were: Four septic embolic cases of endocarditis, two of encephalomyelitis gummosa, one due to malignant tertian malaria, two of circumscribed encephalitic lesions due to a mould (Bonne et al. 1948), one possible postvaccinal case in a soldier acquired on the ship coming from Holland, recently described by Bras and me (Bras 1947), and 3 cases yet to be described.

The encephalitis in the Dutch soldier, already described by Bras and me, occurred 9 days after vaccination against smallpox on board the ship from Amsterdam to Batavia, death supervening 8 days after the onset. Infiltrations consisted of lymphocytes found in the perivascular spaces and a loose

microglia infiltration in the nervous tissue around these vessels. They were much more frequent in the white matter than in the grey one. Most numerous they were in the central part of the cerebral white matter, in the substantia nigra they were absent, in the putamen and the capsula interna they were rare, in the lower parts of the brain-stem a small number of them only were found. In and around the infiltrations ganglion cells looked normal, but in the white matter demyelination was obvious.

The first case of genuine encephalitis to be described was that of a Chinese girl 13 years of age, who on May 23th, 1947, was admitted to the hospital because of a fever of 4 days' duration. One day after admittance she was comatous, the only spontaneous movements she made was a jerking flexion and extension of the right leg and occasional lateral eye movements. She did not speak, all reflexes, the cornea reflexes excepted, were unelicitable, there was no stiffness of the neck, plantars were indistinct. Lumbar puncture yielded clear fluid containing 18 lymphocytes and 2 polymorphonuclears per ccm., the protein content was normal. The girl died at midnight 24th-25th of May. Autopsy was performed 10 hours after death, only the brain was taken out.

The brain was hyperaemic at the outer side as well as on a cross section, the leptomeninx was somewhat opaque, there were neither hemorrhages nor softenings. Frozen sections as well as celloidin embedded slides from all parts of the C. N. S. were stained with hematoxylin and eosin and Spielmeyer's or Weil's myelin sheath-technique, a great number of sections being examined. Infiltrates were found everywhere around medium-sized vessels, consisting of thick cuffs of lymphocytes and a few plasma cells with a loose infiltration of Hortega glia cells around them in the nervous tissue. They were predominantly found in the grey matter and in the white matter almost exclusively very near the gray one, e.g. the subcortical area of the cerebrum, around the lenticular nucleus in the external capsule, never in the core of the large fiber tracts nor in the centre of the cerebral and cerebellar white matter.

Inflammation was most severe in the thalamus, especially dorsal and dorsolateral to the frontal part of the red nucleus and Forel's field H. The wall of the third ventricle was less severely affected, a small number of infiltrated vessels were present, and occasionally Hortega glia proliferation was obvious, but whole areas of unchanged tissue were found. The substantia nigra and the red nucleus were somewhat more affected than the wall of the third ventricle, but apparently less so than the thalamus. In the thalamus a number of hyaline round corpuscles surrounded by microglia cells were found, suggesting the remnants of degenerated ganglion cells, besides this neither special infiltration around ganglion cells nor conspicuous degeneration was noticed. Especially in the substantia nigra the large pigmented ganglion cells were normal in number and aspect, no loose pigment was found in the tissue.

In the corpus striatum changes were pronounced at the boundary of the putamen and the pallidum, on the basal side of the putamen, at Reichert's substantia innominata, and occasionally on the inner side of the external capsula. In the cerebral hemispheres inflammation was predominantly found in the deepest layer of the cortex and in the subcortical white matter, occasionally it was present in the third layer. Hortega glia proliferation was everywhere seen with the cortex, besides this there were nodules of irregularly shaped enlarged Hortega glia cells in small numbers. Neurons were in general numerous and regularly arranged, in some areas, especially the third layer, they seemed to be destroyed. However, there were many sections of the cortex cerebri that hardly showed any change. In the cortex cerebelli no changes were noticed. In the pons and the medulla perivascular infiltrations and Hortega glia proliferation were especially marked in the reticular substance, while the motor nuclei were relatively free and their neurons normal in appearance. In the basal pontine nuclei a few perivascular infiltrates were present. In the first segment of the cervical cord, the only one available, some Hortega glia proliferation was found within and around the posterior horn,

it was much less in the anterior horn; the white matter and the anterior and posterior root fibres were free.

Occasionally infiltrated vessels were found in the leptomeninx, especially on the basal side of the brain near the substantia innominata; diffuse infiltration of the leptomeninx was absent. Spielmeyer stained sections showed no marked demyelination around the infiltrated vessels, in places of rather strong Hortega glia proliferation a number of myelin sheaths were somewhat irregularly shaped, but typical myelin degeneration was nowhere found. Proliferation of neuroglia and fibrous gliosis were absent.

In this case a young Chinese girl, who presumably had always lived in Batavia, presented a short disease with fever and drowsiness that within a few days ended fatally. The only more or less typical feature was a slight pleiocytosis in the spinal fluid. Signs of an infectious disease were not found. An encephalitis was found, characterized by perivascular infiltrates consisting of round cells with a few plasma cells surrounded by loose proliferation of Hortega glia cells within the nervous tissue. This inflammation was found everywhere in the grey tissue the cerebellum excepted, and in the white matter in the neighbourhood of the grey matter. The thalamus, the red nucleus, and the substantia nigra were most severely affected, myelin degeneration and plasmatic or fibrous gliosis were absent, motor neurons were not particularly affected, neither was the grey matter around the third ventricle.

The second case was that of a young Dutch private, born March 20th, 1925, who arrived at Batavia in the beginning of 1947. November 17th and 18th, 1947, he had a chill and fever and was admitted at the military hospital on the 18th. He had no diseases during his sojourn at Java, the last 1½ months he took 1 tablet of mepacrin daily. In the evening of the 18th he showed an epileptic fit or something like it, was confused, semicomatous, and had a stertorous respiration for a short time, the plantar reflex on the left side being in extension. Later in the evening he had another seizure, lumbar puncture was performed and 368 cells per ccm. were found, 15 per cent.

of which were polymorphonuclears. No microorganisms were found.

In the blood no malaria parasites were present. The next day he was confused and restless, had stiffness of the neck, diplopia, impaired lateral gaze and paresis of the left corner of the mouth. Deep reflexes were normal on the right side, unelicitable on the left, plantars were in extension on both feet. Lumbar puncture the next day showed 60 cells per ccm 75 per cent. of which were mononuclears. The patient grew more and more drowsy and confused, the right corner of his mouth was paretic, he was incontinent of urine, death supervened on the 22nd of November at 0.15 hour, 4½ days later his first symptoms. Autopsy was performed 13 hours later by Dr. N. Bossinga at the First Military Hospital. In the internal organs no distinct changes were found, the brain fixed in formalin was brought to my laboratory a few days later. Macroscopically no changes were present, microscopical examination was done in the same way as in the previous case.

Inflammation was found almost exclusively in the grey matter, it consisted of cuffs of lymphocytes and plasma cells around a relatively small number of medium-sized and large vessels and a much more widespread infiltration with enlarged Hortega glia cells in the nervous tissue itself. Besides this there were a number of rarefied areas, in the most affected areas especially the thalamus and the cortex cerebri and a few dense nodules of degenerating Hortega glia cells. The majority of the inflammatory manifestations, however, consisted of rather extensive areas of Hortega glia proliferation, also occurring in zones where perivascular infiltration was absent or rare. The most severely affected area was the thalamus with many Hortega glia cell infiltrations, many rarefied areas and remnants of degenerated neurons. The walls of the third ventricle were not free, but they were definitely less severely affected than the thalamic nuclei. Perivascular infiltration was only rare, even in these severely inflamed areas. Next to the thalamus in severity of affection were the substantia nigra and the cortex cerebri.

In the former general severe Hortega glia proliferation was the outstanding feature, with some degeneration of neurons. In the cerebral cortex general Hortega glia proliferation was moderate, but there were many circumscribed areas in which it was rather dense and in some very dense, rarefied areas it was present in a few slides. Perivascular infiltrations were rare, they were confined to a few medium-sized vessels, in many affected areas they were absent. Neurons were preserved in large numbers; in the rarefied areas they were degenerated, in other zones they were usually normal. In the motor zone changes were only slight.

In the putamen changes were about identical to those in the cerebral cortex, in the globus pallidus they were less severe, rarefied zones were absent. At the boundary of the putamen and the capsula externa a few large vessels showed a dense infiltration of their V. R. spaces.

In the cerebellar cortex the molecular zone showed a small number of areas of Hortega glia proliferation, the Purkinje cells in such areas were now shrunk, now entirely normal; the central nuclei were not affected. In the brain-stem diffuse Hortega glia proliferation was found in the reticular substance, a few Hortega glia cell nodules were found both in the and in the motor nuclei, the neurons were not much affected. The basal pontine nuclei were affected in the same way as the reticular substance. In the first cervical segment of the cord a few Hortega glia cells nodules were found both in the anterior and the posterior horn. The leptomeninx was not generally infiltrated; a number of vessels showed infiltration with the same cells as those in the brain, there were areas in which the pia mater itself also was inflamed, but other areas very close to severely inflamed cortical zones were unaffected.

In this case also there was a disease without distinct neurological symptoms that in a few days ended fatally.

There were two epileptic seizures and signs of meningitis with pleiocytes, initially chiefly of polymorphonuclears, later of mononuclears. In the C.N.S. inflammation was found in

about the same distribution: thalamus, substantia nigra, and cortex cerebri were most severely affected. In this case the cerebellar cortex was not free, inflammation was almost completely confined to the grey matter and perivascular infiltration was much less generally found.

A similar postmortem picture was found in a Chinese boy who was admitted to the Hospital February 26th, 1940, when 8 months of age, and died the next day. He had been ill only one day at home, he showed rigidity of the neck, strabismus, convulsion and high fever, his deep reflexes were hyperactive, tonus was increased, the plantar reflexes were in extension. In the fluid protein was increased; there were 65 lymphocytes and 2 polymorphonuclears per cmm, but no microorganisms. In the brain infiltrations of Hortega glia cells were found in most of the grey areas, with rarefied spots, specially in the thalamic nuclei and the white matter in its vicinity. The basal ganglia and the cortex cerebri were less affected than the thalamus; still Hortega glia proliferation was conspicuous. In the pons and the medulla scattered foci of inflammation were found in the reticular substance. A very large one situated medially to the restiform body, consisted of Hortega glia cells and around some of the vessels a small number of compound granular cells. There was in that focus no perivascular infiltration, but on several spots, especially in the white matter adjacent to inflamed grey areas, medium-sized vessels were surrounded by lymphocytes and larger round cells. Ganglion cells were not especially affected; many of them in the middle of infiltrated areas had a normal aspect. In the inferior olives and the dentate nuclei Hortega glia cell nodules were present in small numbers, in the cord a few small foci of infiltration were found in both horns. The pia mater was normal, myelin sheath staining technique (Loyez) showed partial demyelination around infiltrated vessels.

In this third case inflammation was less extensive than in the previous ones, it showed some affection of the white matter only in the vicinity of grey areas as in the first case and a prevalence of Hortega glia infiltration as in the second case.

In all three cases the course was very rapid, death supervening within a few days after onset, in neither of the cases a concomitant infectious disease was found, the histological picture after death being almost identical in all three cases. The possibility that the same kind of encephalitis in all of them was present is presumable, and the anatomical picture is the only guide available.

A fourth case of real encephalitis, though insufficiently examined and therefore hard to define, was that of the Mena-donesian (N. Celebes) soldier L., 18 years of age, who fell ill July 7th, 1947, with drowsiness, rigidity of the neck, hyperactive deep reflexes and high fever. July 15th he showed catatonia, athetoid movements, and very high deep reflexes. In the fluid the protein content was increased, but no pleiocytosis was found. Death occurred August 1st, 24 days after the first symptoms developed. Unfortunately Dr. Bonnet of the hospital of Tomohon, who performed the autopsy only sent 3 small pieces of brain tissue, a piece of the left half of the pons, a small piece of the cortex cerebri, and one of the dentate nucleus and adjacent lamellae. In the tegmentum pontis some vessels were surrounded by cuffs of small round cells and microglia proliferation was present in the adjacent nervous tissue. In the pes pontis and the cortex cerebri only a slight hypertrophy of the microglia was noticeable. In the dentate nucleus some perivascular infiltration and in the adjacent white matter a few microglia nodules were present.

Therefore an encephalitis of mixed polio-leuco-localisation certainly was present, possibly related to the ones described.

DISCUSSION

As postinfectious encephalitis may be excluded, the types of encephalitis to be considered is the group of encephalitis epidemica A and B and the equine encephalitis. The original v. Economo's encephalitis epidemica A can be discarded as it has not occurred in an acute form during the last two decades and as in it inflammation consists chiefly of peri-

vascular lymphocytic infiltrates in the substantia nigra and the wall of the third ventricle. The Japanese summer encephalitis and the various kinds of probably related encephalitides occurring epidemically in the U.S. since 1933 deserve to be considered most as their anatomical picture in the majority of the cases is essentially the same as in my cases. Equine encephalitis on the other hand is much more localized in the white matter, and more of the necrotizing kind. Moreover, the neuroglia shows hyperplasia and hypertrophy to a degree seen in experimental intoxication.

The histopathology of the St. Louis epidemic was described by Löwenberg and Zbinden (1936). Perivascular infiltrations were found in all parts of the brain consisting of lymphocytes, some polymorphonuclears and monocytes, but perivascular proliferations of Hortega glia cells, mostly without lymphocytes or plasma cells, were much more numerous. Inflammation was most severe in the grey centres of the mesencephalon and in the diencephalon. In the medulla and the pons the cranial nerve nuclei, the reticular substance, the olives, and the basal nuclei showed inflammation. In both the cerebrum and the cerebellum the cortex as well as the white matter in all its parts showed a great number of infiltrated areas.

In the bulletin 214, 1935 of the Public Health Service, Washington, changes in B encephalitis of the 1933 St. Louis epidemic are summarized, they consisted of perivascular infiltrations with lymphocytes and plasma cells and Hortega glia nodules. In half of the cases large areas of nervous tissue were infiltrated with Hortega glia, two thirds of them showed Hortega glia nodules: degeneration and changes of ganglion cells were almost always present, perivascular demyelination was absent. All parts of the C. N. S. were affected, leptomeningitis was always present, the cerebral cortex and the brain-stem nuclei showed the strongest changes.

An epidemic of Japanese encephalitis occurred among U. S. military personnel and the native population on the Okinawa-Jima Ryukyu Islands in 1945. Lewis, Taylor, Sorom, Norcross, and Kindsvatter (1947) gave an elaborate description of the

clinical features, and a summary of the anatomical changes. Softening to frank cystic degeneration was found in the grey matter of the mesencephalon and the pons, and in focal areas of the cerebral and the cerebellar cortex but only in cases that died 38-52 days after the onset of the disease.

Zimmerman in 1946 described the pathology in the same epidemic more elaborately, 2 of U. S. military personnel and 9 natives died in 5-52 days after the first symptoms had appeared. The cases that died within two weeks after onset showed infiltration of the pia mater with sparse lymphocytes, foci of ring hemorrhages and capillary congestion in the basal ganglia, and perivascular cuffing by lymphocytes, mononuclears and macrophages in many different parts of the brain, including the white matter, especially in the cord. Neuronal destruction was conspicuous in the cerebral cortex, the basal ganglia, the pons, the medulla, the cerebellum, and the cord, the degree varying from case to case and from zone to zone. They were at times accompanied by infiltration of neutrophil leucocytes and by proliferation of Hortega glia cells. In the anterior horns changes resembled those of poliomyelitis, neuronophagia infiltration with polymorphonuclears and Hortega glia proliferation. A spongy condition developed when large numbers of neurons disappeared in the cortex cerebri and the substantia nigra.

Haymaker and Sabin (1947) described the case of an American soldier who died of the disease August 7th, 1947, 11 days after falling ill. There was a mild leptomeningitis infiltration consisting of lymphocytes and histocytes. Nodules and perivascular cuffs of lymphocytes were found in the substantia nigra, the nodules were confined to the grey matter, the cuffs were also present to a limited degree in the sub-cortical matter. In the cortex they were closely related to degenerated or necrotic neurons, and to the walls of the blood vessels. Hortega glia was absent from the nodules, but some of the cells in the parenchyma bore a resemblance to it. The cerebral white matter was but little affected, nodules were most numerous in the region of the fossa sylvii, the tip of the

temporal lobe and the hippocampus, they were found in all layers. The thalamus and the substantia nigra were most heavily affected, numerous neurons had disappeared, the basilar nucleus and the globus pallidus were somewhat less affected, as were the adjacent nuclei of the diencephalon and the mesencephalon. Other grey centres were still less affected, the white matter was relatively free. The molecular layer of the cerebellar cortex showed numerous nodules, diffuse infiltration chiefly of Hortega glia was found from the Bermann glia layer on to the pia mater, especially where the Purkinje cells were damaged.

Previous papers on this encephalitis are those by Bertrand and Miyasita (1936). Besides the changes described they found numerous foci of demyelination in the whole of the brain-stem and the myelum of the cerebral gyri. Höra in 1939 described a case of Encephalitis japonica in Germany in a boy 6 years of age, in whom affection of the white matter of the cerebral and cerebellar hemispheres as well as the brain-stem prevailed.

Hashimoto and Kudo reported cases in natives and Europeans in Tokyo in the autumn of 1935; encephalitis was predominantly found in the brain-stem and the basal nuclei.

This short review of encephalitis japonica shows distinctly that the changes differ from case to case, that they differ according to the acuteness and the duration of the disease and that it is hard to summarize its features. One of the outstanding characteristics is a negative one, it is not a typical leuco-encephalitis with proliferation of the neuroglia and conspicuous demyelination as postvaccinal encephalitis usually is, and the cases described as disseminated encephalomyelitis, acute forms of multiple sclerosis and the like. It is distinguished from the best-known polio-encephalitis, v. Economo's encephalitis, by a much more general inflammation, not confined to the wall of the third ventricle and the mesencephalon, especially the substantia nigra.

In varying degree these conditions are fulfilled in three of the cases, while in the fourth examination was too restricted

to give a clue. Perivascular infiltration was present in all of them, but Hortega glia proliferation was prevalent; the grey matter was chiefly and most severely affected, but the white matter was not completely intact. The substantia nigra and the thalamus were most severely affected, all of the grey centres of the brain-stem participated in it with the cerebral cortex and in one case, though to a much lesser extent, the cerebellar cortex. It is clear that when an anatomical picture can give sufficient evidence for diagnosis and no other encephalitides exist than as yet are known, the described cases must be assumed to belong to the encephalitis B group. The three cases described occurred at different times in different classes of people, and in between no clinical cases of encephalitis were noticed. Until serological reaction and inoculations in susceptible animals have been performed, no absolutely certain diagnosis can be made.

SUMMARY

A review of cases of encephalitis at Batavia since January 1931 is given. Only cases controlled by postmortem examination of the C. N. S. are recorded. Only four certain and one probable case of genuine encephalitis were found in 1,040 microscopically examined specimens of the C. N. S.

All the five cases were predominantly polio-encephalitides, three of them with relatively moderate participation of the white matter.

The anatomical picture in three cases pointed to relationship with the Japanese summer encephalitis and that of the St. Louis type.

Possibly an encephalitis of this type is endemic in this country.

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INVESTIGATIONS INTO THE COLOUR-FORM REACTION OF EPILEPTICS

BY

IVAN BLOMQVIST

The general psychological observation that certain persons are more apt to observe the form and others the colour of objects perceived (*Külpe, Kuhlman, 1904*) soon became the point of departure for investigations from the standpoint of genetic psychology (*Descouedres, 1913; Katz, 1913, et al.*). It was not until later that investigators commenced to take notice of the characterological aspects of this phenomenon (*Scholl, 1927; Dambeck, 1929; Lutz, 1929; Ritter, 1930; Lindberg, 1938*).

Only a few investigators have taken up for treatment the problem of the influence of mental disorders on colour-form reaction. *Lindberg*, for instance, has examined not only children of school age but also adults presenting different symptoms of psychic insufficiency, determined according to *Sjöbring's* typology. In point of fact these investigations should therefore be assigned to the above-mentioned typological research group. Of other mental disorders only schizophrenia and epilepsy have been subject to the study of colour-form reaction. This may seem somewhat remarkable, but the explanation probably lies partly in the circumstance that the epileptic morbid conditions and schizophrenia so often affect the personality and involve pronounced changes in character.

The colour-form reaction of schizophrenics has been investigated by *Lindberg* with his Ring Test; the colour reaction, he found, increased parallel with the relative severity of the schizophrenia. The mild incipient cases of schizophrenia showed roughly the same percentage of colour reaction as the patients in a surgical department, whereas the severe cases of dementia praecox presented the most pronounced colour reaction, over 82 per cent reacting in this way. An even stronger colour reaction was exhibited by 25 patients with the diagnosis *Insania et dementia presenilis et senilis*. These results tally with the findings of investigators who have worked with the Rorschach method (*Enke; Skalweit*).

The colour-form reaction of epileptics has been illustrated by *Stauder* and *Weissenfeld*, by investigations with the Rorschach method. *Stauder* considers that colour responses are not characteristic of genuine epilepsy, in which he obtained pronounced colour responses in only 31 per cent. On the other hand he found them to be very common in the so-called residual epileptics, wherefore he drew the conclusion that explosive affectivity does not occur so generally in genuine epilepsy as is usually supposed. *Weissenfeld*, on the other hand, found that the genuine epileptics had poor form perceptibility, which he regards as a sign of dementia, both congenital and acquired. Colour response occurred in 60 per cent of genuine epileptics (50 patients examined), and was therefore a common though not obligate symptom. In hypersensitive epileptics in whom no severe forms of dementia or imbecility were demonstrable, there was no sign of the triad of poor form perception, confabulation, and perseveration which occurs in genuine epilepsy. Nor was any purely colour response obtained, though in a few individual cases colour-form or form-colour responses.

In every experimental psychological investigation of epileptics due consideration must be paid to the fact that many epileptics present major mental derangements, partly in the form of primary defective conditions and partly in the form of changes developing in connection with the disease. Pre-

viously the incidence of such derangements was widely regarded as very high. Even *Esquirol* (1838), for instance, considered that four fifths of his epileptic patients were more or less mentally deranged. *Kraft-Ebbing* held that the psychic functions in most cases of epilepsy were permanently impaired. *Kraepelin* demonstrated that in genuine epilepsy there usually develops a more or less pronounced special change of personality. *Bleuler* was of opinion that persons with epilepsy as a rule are psychopaths, even before the disease has left its characteristic mark on them, and that specific mental characteristics are associated with epilepsy. These usually increase parallelly with the duration of the disease. According to *Bleuler* one may speak of epileptic character, epileptic psychopathic constitution and, in severe cases, epileptic dementia, according to the severity of the psychic changes. *Pilcz* considered that protracted epilepsy, except in very rare exceptional cases, results in certain permanent psychic anomalies, frequently so pronounced that a diagnosis can be made on the basis of them. *Muskens*, finally, considered that mental changes were almost invariably associated with epileptic attacks over a considerable period of time.

Judging by a number of recent investigations, however, it would seem that this generally accepted view needs revising. *Paskind* thus found that of 304 private patients suffering from epilepsy with a duration of 6 years or more, only 6.5 per cent showed mental changes, the others working in ordinary occupations, some of them being qualified professional men such as bank managers, teachers, physicians, etc. *Lennox*, in examining non-hospitalized patients with epilepsy, found that 45 per cent were mentally normal despite the fact that they had been afflicted for more than 20 years. Finally, *Bridge* contends that "in the majority of patients deterioration is not apparent even after many years." Hence the result arrived at in regard to the frequency of mental derangements in epilepsy would seem to depend on the nature of the case material, and primarily on the question whether the patients are institutionalized or not. The logical explanation of this lies in the fact that the

indication for hospital or institutional care is not solely, or even in great part, determined by the epilepsy as such but by other factors partly existing in the patient himself and partly of a medico-social nature. Thus rational ambulatory treatment is frequently rendered difficult or even impossible by unsuitable and unsatisfactory environmental conditions. Moreover, institutionalization is often necessitated by abnormal behaviour on the part of a sick person, due to mental changes.

Judging by the relevant literature, only a few investigations have been carried out for the express purpose of elucidating the intellectual developmental level of epileptics. *Löwenstein* tested 16 cases with the Yerkes-Bridges intelligence test, finding only six of them to be subnormal. *Fox*, in examining the 150 children between the ages of 5 and 17 institutionalized at Longfield Epileptic Colony, obtained a mean I.Q. of 71 for boys and 65 for girls; and *Dawson* and *Conn* obtained a mean I.Q. of 80.7 for a group of 49 children. *Barnes* and *Fettermann*, in 105 epileptics under ambulatory treatment, found a mean I.Q. of 74, with variations ranging between 35 and 130.

These authors have also conducted interesting investigations into the development of epileptic children's intelligence by testing them at certain intervals. *Fox* thus found a general tendency for the intelligence level to fall, though it was fairly pronounced only in 8 per cent. *Dawson* and *Conn*, too, found "definite evidence of deterioration", albeit varying widely in individual cases and being altogether absent in some. The variability was much higher than in other patients. *Barnes* and *Fettermann* found fluctuations from test to test. Only one of 35 patients examined showed a constant fall in the intelligence level, and five showed a constant rise. Employing Babcock's test, they found a slight tendency for the intellectual level to fall, though it was neither significant nor of any pathological importance. Finally, *Kugelmass*, *Poull* and *Rudnick* carried out intelligence tests on 129 institutionalized epileptic children and 91 epileptic children treated privately, estimating the development of their intelligence by means of serial tests. The institutionalized children, they found, "were retarded mentally" in

relation to those treated privately. This backwardness, however, remained within the intelligence limits of non-selected backward hospitalized children without epilepsy.

To sum up these investigations into the mental derangements of epileptics, it may be said that the incidence of such derangements probably has been considerably exaggerated in the past, but that at all events it is high in the institutionalized epileptics and that these latter exhibit especially a conspicuous impairment of intelligence. It would be inappropriate here to discuss the causes or the nature of this; suffice it to say that investigations conducted hitherto have failed to demonstrate any definite correlation between intellectual development and frequency and severity of attacks, and that no general and progressive decline in the intelligence quotient has been found. In those cases in which such a decline has been established, it has appeared to be correlated with the general condition or with the duration of the disease.

Through a study of the relevant literature, together with the author's own observations of the case material intended for investigation, it was therefore found necessary to undertake a systematic determination of intelligence with the object of elucidating whether the intellectual development had any influence on the colour-form reaction. On this particular point the views of earlier investigators have diverged.

Scholl did not gain the impression that those presenting form reaction were particularly intelligent, but held no definite view and advocated further investigations. *Descouedres* obtained identical results at high and low levels of intelligence. *Ritter* contended that intelligence was of no importance in his experiments, since the two types of reacting subjects included persons both of high and low intelligence. His figures, however, show a somewhat lower percentage of colour responses among children in relief classes than among other children of corresponding ages. *Tobie*, on the other hand, considered that form reaction increased with the development of intelligence; and *Engel*, too, found a relationship between the choice of colour or form and the intelligence. Finally, *Lindberg*

found that the percentage of initial colour responses was correlated in some measure with the intelligence. The least intelligent children at the elementary school stage presented a somewhat more marked tendency to initial colour response than the most intelligent children.

OWN INVESTIGATIONS

The present material comprises 103 male and 110 female patients, institutionalized at the State Institution for Epileptics, Vilhelmsro. The determination of intelligence was carried out with Wåhlén's Swedish translation of "A Point Scale for Measuring Ability", by Yerkes, Bridges, and Hardwick. In examining the intelligence of epileptics it is necessary to pay special attention to the slowness of their mental reactions. Hence, tests at specific intervals are not altogether suitable if the aim is to elucidate the capacity of these patients independently of time factors. In this respect the method employed involves definite advantages, for only one test incorporated in it embodies a time factor, namely the test consisting in the drawing of figures from memory, in which the objects are permitted to be viewed for 15 seconds. In those cases in which a bradypsychic type of reaction was demonstrated, the author prolonged the exposure to 20 seconds, and in other tests allowed as much time for responses as the subjects needed. Where no responses at all were obtained, questions were put with the aim of ascertaining whether the subject had any reply to offer. All intelligence tests, like the colour-form tests, were conducted by the author himself. They were performed in close connection with the colour-form investigations, but *after* these latter—this in order to secure as objective an evaluation of the colour-form reaction as possible. The author also avoided making examinations in connection with epileptic attacks or when the patients were in a state of confusion.

The result of the intelligence investigation emerges from Table 1. The distribution between different I.Q. groups is fairly uniform for both sexes. By evaluating each sex separately

TABLE 1.
Distribution of Intelligence Quotient.

I. Q.	Number		
	Males	Females	Total
20-30	2	1	3
30-40	4	11	15
40-50	11	14	25
50-60	25	20	45
60-70	20	22	42
70-80	15	12	27
80-90	11	9	20
90-100	7	6	13
100-110	4	11	15
110-120	3	4	7
120-130	0	0	0
130-140	1	0	1
All I.Q. groups	103	110	213

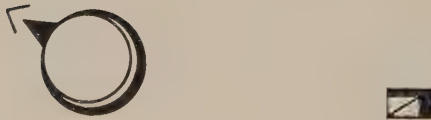
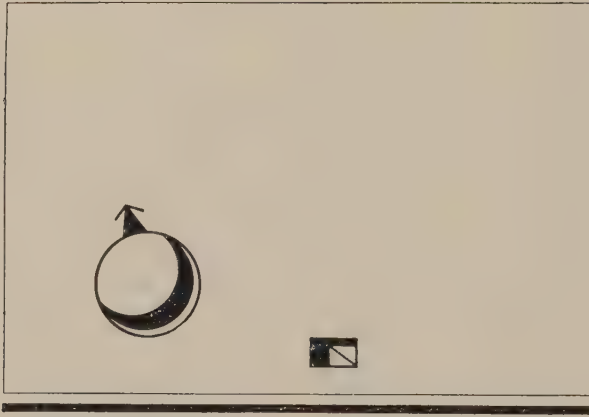
a mean I.Q. is obtained of 67.3 ± 2.01 for the male subjects and 67.0 ± 2.13 for the females. Since the discrepancy between these two values is inappreciable, it is warranted to calculate the mean I.Q. of the material in its entirety, the resultant value being 67.1 ± 1.5 . Thus the intelligence quotient as a whole is low, but presents considerable variations. The mean I.Q. relative to various age groups emerges from Table 2.

The examination of the colour-form reaction was carried out with Lindberg's Ring Test. The material for this latter

TABLE 2.
Mean Intelligence Quotient at Various Ages.

Age	I. Q.	M	No.
6-10 years	80.3	7.3	12
10-14 „	65.3	5.6	43
14-18 „	74.7	3.4	40
18- „	60.5	1.8	118
Entire series	67.1	1.5	213

consists of two cards of uniform size, 15.5×10.4 cm, placed on the same page and of the general appearance shown in Fig. 1. The examination itself involves the exhibiting of this page to the subject, the card with the blue figures lying uppermost. The following guidance is then given verbally: "Here



you have two rings. As you will see, they are not alike. In what way do they differ?" When the subject has given a reply, the investigator asks: "Do you observe any other differences?" If the subject hesitates or seems incapable of grasping what the task implies, further instructions are sometimes necessary. The experiment concludes when the subject gives no further replies or is unable to detect any further differences.

In evaluating the results, Lindberg classifies those persons who in their first or second reply have emphasised the difference in colour as "colour reagents", and calls their replies

"initial colour responses". But the employment of this method of evaluation, in the present writer's opinion, seems to enhance the changes of colour reaction at the expense of other reactions. Thus, if a subject should first give a form response and thereafter a colour response, Lindberg calls this reaction, too, an initial colour response, though in the author's opinion it should be classified as an initial form response. Lindberg, in his works, has not given any basis for his evaluation procedure. Possibly he has deemed the colours in his test to be of such minor importance in relation to the differences in form that he has wanted to enhance the possibilities for the colour reaction to be conspicuous. This, however, can scarcely be the true explanation; on the contrary. In this connection, Lindberg himself states that the colours are "*hervorragend klar*". The test, it is true, embraces only one colour difference but several other dissimilarities, including several in form; but on the other hand the differences in form are in themselves less pronounced than the colour difference.

However, to make possible a comparison with Lindberg's material the present writer has made calculations also according to Lindberg's evaluation procedure.

In studying the colour-form reaction in a case material showing variations in intelligence development, it is necessary to take into account the age distribution, too, since the colour-form reaction, as we have seen, involves a genetical factor. Hence the material must be divided up with due consideration to both age and intelligence quotient.

The data collocated in Table 3 now show that the number of initial colour responses is greatest in the group with I.Q. <50 . This applies both to male and female subjects; for 20 (74 per cent) of the 27 females and 12 (75 per cent) of the 16 males presented initial colour responses. In I.Q. groups 50—90 and >90 , considerably lower values were obtained, as will be seen from the table: 36 and 58 per cent, respectively, for the female subjects, and 51 and 50 per cent, respectively, for the males.

In examining the colour reaction in the various age groups

TABLE 3.
Initial Colour Responses.

Age	I. Q.							
	-50		50-90		90-		Total	
	abs.	%	abs.	%	abs.	%	abs.	%
Females:								
10-14 years	2/2		4/6				6/8	75
14-18 "	1/1		3/13	23	5/8		9/22	41
18- "	17/24	71	16/45	36	6/11	55	39/80	49
Entire series	20/27	74	23/64	36	11/19	58	54/110	49.1
Males:								
6-10 years	1/1		5/7		4/4		10/12	83
10-14 "	1/1		16/28	57	1/6		18/35	51
14-18 "	1/2		4/14	29	0/2		5/18	28
18- "	9/12	75	11/22	50	3/4		23/38	61
Entire series	12/16	75	36/71	51	8/16	50	56/103	54.4

the number of individuals in general is found to be too small to afford any possibility of a reliable comparison. Only in the age group consisting of eighteen-year-olds and over the number of subjects is large enough to yield statistically certain values. The percentage of colour reagents here, it will be seen, is almost identical with that of the material in its entirety—and this even in the different I.Q. groups. The much higher percentage of colour reagents in the group of male subjects with I.Q. 50-90 than in the corresponding female group (51 and 36 per cent, respectively) seems to be partly due to the considerably lower average age of the male subjects. Among these latter, the group comprising ten- to fourteen-year-olds represents approximately 40 per cent of the entire group, as compared with only about 10 per cent among the females.

The influence of age on colour reaction is difficult to judge owing to the scarcity of material in the various age groups. It is noteworthy, however, that the 14 to 18 years age group shows the lowest percentage of initial colour responses.

TABLE 4.

Initial Colour Responses According to Lindberg's Calculation Method.

Age	I. Q.							
	-50		50-90		90-		Total	
	abs.	%	abs.	%	abs.	%	abs.	%
Females:								
10-14 years	2/2		4/6				6/8	75
14-18 „	1/1		6/13	46	6/8		13/22	59
18- „	17/24	71	23/45	51	7/11	64	47/80	59
Entire series	20/27	74	33/64	52	13/19	68	66/110	60.0
Males:								
6-10 years	1/1		5/7		4/4		10/12	83
10-14 „	1/1		18/28	64	2/6		21/35	60
14-18 „	1/2		5/14	36	0/2		6/18	33
18- „	11/12	92	17/22	77	4/4		32/38	84
Entire series	14/16	88	45/71	63	10/16	63	69/103	67

In this age group the mean I.Q. is highest (74.7), with the exception of the 6 to 10 years age group, in which the material, however, is not very copious.

No certain and significant difference is demonstrable between male and female subjects. The adult males include a larger number of colour reagents, the contrary being the case among younger subjects.

Since the mean intelligence quotient in the material investigated is virtually the same for male and female subjects, it should be permissible to compare the percentages of all male and female subjects presenting colour reactions. These figures amount to 49.1 ± 4.76 per cent for the females and 54.4 ± 4.9 per cent for the males, the mean difference being 5.3 ± 6.8 per cent. Thus no definite statistical difference exists between the male and female subjects in the material as a whole.

In principle the same reaction tendency is obtained when the calculations are made according to Lindberg's method of

TABLE 5.
*Initial Colour Responses (All Males and Females) According to Lindberg's
 Calculation Method.*

Age	I. Q.							
	—50		50—90		90—		Total	
	abs.	%	abs.	%	abs.	%	abs.	%
6-10 years	1/1		5/7		4/4		10/12	83.3
10-14 „	3/3		22/34	65	2/6		27/43	62.8
14-18 „	2/3		11/27	41	6/10	60	19/40	47.5
18- „	28/36	78	40/67	60	11/15	73	79/118	66.9
							135/	
Entire series	34/43	79.1	78/135	57.8	23/35	65.7	213	63.4

evaluation (Table 4). However, the values of the initial colour responses, as was to be expected, are higher here than according to the author's method of calculation. The proportion of colour reagents is thus 11 per cent higher for the females and 13 per cent higher for the males. For the material as a whole the difference amounts to 11.7 ± 4.7 per cent, and may thus be regarded as statistically probable, amounting as it does to over twice the mean error. In the lowest intelligence and age groups the number of colour reagents shows either no increase at all or only a very inappreciable one. This circumstance may be considered to indicate that at a low degree of mental development the tendency to colour response is more dominant, wherefore such a response is obtained already in the initial reply.

But as far as our efforts to gauge the colour-form reaction of epileptics are concerned, neither the absolute nor the percentage figures obtained are of much benefit in themselves; comparisons are necessary with normal material, investigated with the same methods. In this connection, however, only the juvenile and surgical material investigated by Lindberg is available. The juvenile material derives from normal classes in Malmö elementary schools and is not divided into I.Q. groups, though a certain classification according to ability

TABLE 6.
*Comparison between the Author's Material and Lindberg's Surgical
 Case Material.*

	No.	Init. col. resp.	
		abs.	%
Lindberg's surgical material	218	47	21.5 ± 2.8
Adult epileptics with I.Q. 90 and over	15	11	73.3 ± 11.4
All adult epileptics	118	79	66.9 ± 4.3

has been undertaken. Since the mean I.Q. in the author's epileptic material is so low, even in the children's groups (see Table 2), it would be inadvisable to make comparisons between the colour reaction of these epileptics and that of the children of corresponding ages in Lindberg's material: the disparities in the intelligence level might influence the results. Only the 90—I.Q. group could be utilized for comparison with normal material, but here the author's juvenile groups are too small.

In the age group comprising subjects of eighteen years and over, the material is somewhat more copious, so that a comparison with Lindberg's surgical material may be ventured (Table 6). If all epileptics aged eighteen and over are included regardless of intelligence level, we obtain, owing to the lower colour reaction in the 50-90 I.Q. group, a somewhat lower percentage of initial colour reagents (66.9 per cent), though this figure is in the region of that obtained for the higher I.Q. group (73.3 per cent). At all events we obtain a statistically certain and substantial preponderance for the initial colour responses in adult epileptics in comparison with normal subjects (66.9 per cent and 73.3 per cent respectively in the epileptics, and 21.5 per cent in Lindberg's surgical material). Thus the difference between the number of initial colour reagents among Lindberg's surgical patients and among the present author's adult epileptics amounts to 45.4 ± 2.7 per cent. If we include only those adult epileptics who show an I.Q. of 90 and over, a difference is obtained of 51.8 ± 3.8 per cent. From this it

TABLE 7.
Distribution of Constitutional Types in Epileptics.

	Westphal's grouping	According to Janz
Athletic	28.9 %	33.3 %
Leptosome	25.1 %	28.5 %
Pyknic.....	5.5 %	4.9 %
Dysplastic	29.5 %	20.6 %
Non-specific	11.0 %	12.7 %

emerges that the adult epileptics, even when their intelligence development is normal, show a highly increased tendency to colour reaction in comparison with normal subjects.

Another factor of importance to colour-form reaction in a group of people lies in the distribution of constitutional types within the group in question. Several authors have investigated colour-form reaction with reference to constitutional type, and have been able to demonstrate typological differences in reaction (School; Dambach; Lutz; Ritter; Poppinga; Oeser; Kibler; Enke; Braat; Schmidt; Lindberg). All of these authors have found a more or less strongly pronounced correlation between colour reaction and cyclothymia and pyknic type, respectively, on the other hand, and form reaction and schizothymia and leptosomatic type, respectively, on the other. Thus *Lindberg*, in his mentally insufficient adult patients, has determined the frequency of initial colour responses in groups of patients with different body types, determined according to Strömngren's index. He found a difference of 28.8 ± 10.6 per cent between extreme index types.

Several investigations have been conducted into the distribution of body types among epileptics. A synopsis of these cases, numbering roughly 1,500, has been made by *Westphal* (comprising works published up to 1931). *Janz's* investigation (1941) of constitution and disposition to convulsions comprises a series of 102 symptomatic and genuine epileptics. He found no essential difference in body type between the symptomatic and the genuine types. From *Westphal's* synopsis and

TABLE 8.

Initial Colour Responses in Lindberg's Mentally Insufficient Patients with Constitution Index ≤ 0.5 and the Author's Epileptic Material with the Same Index.

	Lindberg			Blomqvist			Diff.
	No.	Init. col. resp.	%	No.	Init. col. resp.	%	
Males	53	21	39.6	27	20	74.1	34.5
Females	54	13	24.1	70	42	60.0	35.9
Combined	107	34	31.8	97	62	63.8	32.0
			± 4.5			± 4.8	± 6.7

Janz's material it emerges that only a very small proportion of epileptics are of the pyknic type; the vast majority are athletic, leptosomatic and dysplastic, being more or less evenly distributed between these three types (Table 7).

In the majority of investigated epileptics of eighteen or over, the present writer has determined the constitution index according to Strömgren. Strömgren's index, as is known, ranges between +2 and -2 and serves to differentiate the pyknic from the leptosomatic type components. According to Strömgren, the plus values indicate a pyknic, and the minus values a leptosomatic constitution. The material comprises 116 cases: 35 men and 81 women. They include none with index $\geq +0.5$, and only 3 with indices between +0.49 and +0.05, whereas all the others show a minus index. 16 of these are assignable to the group with indices ranging between +0.5 and -0.49, and 103 to the group ≤ -0.5 . The mean index is -0.9, i.e. a markedly leptosome index. In view of this one-sided distribution of indices in the material it has not been possible to make any comparisons between the relative colour-form reactions in different index groups, as Lindberg has done in his material.

On the other hand a comparison is possible between the index group ≤ -0.5 and Lindberg's insufficiency cases from the Psychiatric Clinic at Malmö, with a corresponding index (Table 8). It will be seen that a substantial difference exists

between the two materials. The frequency of the leptosomatic epileptics' initial colour reaction in its entirety is 32 ± 6.7 per cent higher than that of Lindberg's leptosomatic insufficiency patients. The epileptics, it is true, have a lower intelligence level; but even the epileptics with an I.Q. of 90 and over show a colour reaction percentage almost as high (see Table 5). Hence the cause of the marked tendency towards colour reaction on the part of the leptosomatic epileptics probably lies in factors associated with the epileptic syndrome.

Thus, each of the comparisons which have been made shows that the epileptics have a strongly pronounced tendency towards colour reaction. In cases of epilepsy this should be interpreted, it would seem, as a pathoplastic phenomenon. However, it is assuredly not a specific symptom, but rather has its root in the general "fall in level" which is caused by the disease itself and which, of course, is commonly observed in cases of organic mental disorders.

SUMMARY

The tendency to observe the colour rather than the form, or vice versa, (colour-form reaction) of objects perceived has been the subject of a considerable number of investigations from the standpoints of genetic psychology and characterology. The influence of various mental disorders on this reaction hitherto has been investigated only in schizophrenics and epileptics—in the latter by means of the Rorshach method.

The present writer has studied the colour-form reactions of 213 epileptics ranging from 6 to 55 years of age and institutionalized at the State Institution for Epileptics, Vilhelmsro, Jönköping, Sweden. Since colour-form reaction varies according to differences in intellectual level and constitutional type, both intelligence tests and the determination of constitution were undertaken, in addition to which a survey is given of earlier investigations in this field.

The I.Q. has been determined by means of "A Point Scale for Measuring Mental Hability", by Yerkes, Bridges and Hard-

wick, translated into Swedish by Wåhlén. The mean I.Q. of the entire material was found to be 67.1 ± 1.5 .

The determination of constitution was carried out according to Strömgren on the adult epileptics, totalling 116 cases. Mean index = — 0.9, i.e. a pronounced leptosome index. Only 3 patients showed a pyknic index.

The colour-form reaction was investigated with Lindberg's Ring Test, the resultant initial colour responses being distributed between different intelligence and constitution groups.

Initial colour responses were given by 49.1 per cent of the female patients and 54.4 per cent of the male patients (according to Lindberg's evaluation method, 60.0 and 67 per cent, respectively).

In the under eighteen age groups the material in the different intelligence groups is too scanty to permit of any comparison with Lindberg's material. But on the other hand a comparison is possible between the colour reactions of the adult epileptics (66.9 per cent) and of Lindberg's surgical case material (21.5 per cent). The difference amounts to 45.4 ± 2.7 per cent.

The leptosomatic epileptics exhibit a colour reaction 32 ± 6.7 per cent higher than Lindberg's leptosomatic mentally insufficient patients.

The marked tendency towards colour reaction of the epileptics is regarded by the author as a pathoplastic phenomenon, associated with the general "fall in level", as in the case of schizophrenics.

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THE DURATION OF EXPERIMENTAL
DISTURBANCES IN THE CEREBRO-
VASCULAR PERMEABILITY
DUE TO CIRCUMSCRIBED GROSS
DAMAGE OF THE BRAIN

BY

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(Lund)

In earlier investigations colour indicators have shown that disorders in the cerebrovascular permeability are relatively brief. *Broman* (1940), for example, showed that such a disorder was observable in the pial vessels only for about one hour after a 10-20 minute passage of air or fat emboli. With solid micro-embolism which become lodged in the vessels the disorder in the permeability localized in the immediate vicinity of the emboli lasted about five days (probably longer in cases with fat emboli in which the latter could be displaced later, e.g. by raising the blood pressure). Toxic lesions of the vascular wall such as the suspected allergic lesion produced experimentally in the brains of guinea-pigs by sheep hemolytic rabbit serum (*Forssman*, 1922, 1926; *Skoog*, 1937) lasted up to seven hours. (*Broman & Lindberg-Broman*, 1945). Another type of toxic vascular lesion produced by a certain contrast medium for cerebral angiography (Umbradil forte), was of an especially mild nature and disappeared already after one to two hours (*Broman & Olsson*, 1948). The disseminated cerebrovascular disorder produced in insulin coma and metrazol shock ceased practically immediately after the coma and the shock, respectively, had worn off (*Bjerner, Broman & Swensson*, 1944). In experiments with a disturbance of the cerebrovascular permeability due to local traumatization

and venous stasis occurring in association with cerebral herniation, the disturbance also disappeared almost immediately after the cessation of the pressure (*Broman*, unpublished study).

It was considered important to complement earlier examinations by still another form of experimental lesion, a gross necrosis of the cerebral tissues. Such damage is most readily produced by electrocoagulation (Cf. *Schmid*, 1931). This type of lesion was believed to be worthy of a special study, partly because it is somewhat different from those examined hitherto, and partly because it was considered important to find out whether it was possible for such damage to cause the dural vessels to grow into the damaged zone in association with the later organization process in the necrotic area. If this proved to be the case, it would mean that a permanent pathologic escape of substances from the blood vessels of the scar would be possible—a phenomenon that might be of interest for the better understanding of the physiopathology of scars in the central nervous system.

Examination Results.

Most of the examinations were performed on rabbits and cats. The parietal region of the cranium was trephined on both sides. Electrocoagulation was then performed with the poles over the two trephined openings (dura intact). The animals were then allowed to live for a varying time, after which they were anaesthetized and given an intravenous injection of 0.5 per cent. trypan blue in a saline solution, about 100 ml/2 kg body-weight. The dye was then allowed to take effect for about 10 to 15 minutes, after which the animals were killed and the cranial blood vessels perfused with saline solution to wash out the stained blood, subsequent to which the brain was fixed by a perfusion of a 10 p.c. formalin solution (reference is made to earlier studies—*Broman*, 1941, *Broman & Lindberg-Broman*, 1945—for information concerning technical details).

The results of our examinations will be apparent from the following table and paragraphs.

Exp. No.	Animal	Standing of damage	Disorder of vasc. permeability in damaged region	Adhesions between dura mater and the damaged region
1.	Rabbit	1 hour	+	+
2.	"	1 "	+	+
3.	"	3 "	+	+
4.	"	17 "	+ peripheral	+
5.	"	1 day	+	+
6.	Cat	1 "	+	+
7.	Rabbit	2 "	+	+
8.	Cat	2 "	+	+
9.	Rabbit	1 week	+	+
10.	Cat	1 "	+ ?	+
11.	"	1 "	+	+
12.	"	1½ "	+	—
13.	"	2 "	—	—
14.	"	3 "	—	—
15.	"	1 month	—	—
16.	"	1 "	—	—
17.	Rabbit	4½ "	—	—
18.	"	3 weeks	+ peripheral	+ abscess
19.	"	4 "	+	+

1. The disorder in the permeability of the cerebral vessels is initially demonstrable over the whole of the damaged area. After a few hours, however, the lesion develops centrally in such a manner that complete stasis and destruction of the tissues supervenes, whilst the peripheral vessels are still passable and show a distinct persistent disturbance of their permeability. This condition continues more or less unchanged for about a week, after which the permeability becomes normal in connection with the advancing healing process.

2. In the early stage the damaged cerebral tissue is adherent to the dura mater, which is only natural. Already after about one week, however, there is no longer any union between the brain surface and the dura mater, and the further organization of the necrotic tissues proceeds independent of the dura mater.

3. If an infection should supervene and give rise to a local abscess, the vascular disturbance will persist in the capsule of the granulation tissue (Cf. *Macklin & Macklin*, 1920; *Bro-man*, 1944).

It should be added that during the first week the vessels in the periphery of the damaged area are exceptionally delicate so that stasis and diapedesis may easily occur in association with the examinations described above, even though the damaged area is not subjected to any further direct traumatization.

DISCUSSION

According to what has been revealed by earlier investigations into various types of disorders of the cerebrovascular permeability, it is obvious that even when the parenchyma is relatively grossly damaged (electrocoagulation), the disorder in the permeability is transient. Those vessels located in the centre of the lesion are damaged most and will be the site of a total stasis, the early or late appearance of which will naturally be dependent upon the severity of the damage. With the technic adopted by us stasis in the centre of the damage will not develop immediately, but gradually increase during the first few hours thereafter.

The vessels in the periphery of the lesion will, however, be passable, although they show evidence of a disorder in their permeability for about one week after the occurrence of the lesion. This duration of the disorder is remarkable. One might ask which of the following causes might be responsible for this vascular disturbance lasting for a week:

- 1) a persistent effect of the original thermic vascular damage,
- 2) an effect of the necrotic cerebral substance on the vessels (= toxic effect of autolytic products, "aseptic inflammation"?) or,

- 3) a formation of new vessels, which have not yet developed the permeability peculiar to normal cerebral vessels.

It cannot be decided on the basis of the present investigation which of these explanations is correct. The fact that other forms of damage do not seem to give rise to disorders of the permeability of more than one day's duration, unless the injurious agent is still active (cf. experiments with micro-embolism, cases with brain abscesses or tumours), argues against the first explanation. That in micro-embolic lesions no disorder of the permeability of the vessels located near the small necrotic areas is manifestable, argues against the second possibility (*Broman*, 1940), but on the other hand, the destruction in these small areas is not so marked as in those gross thermic damages produced intentionally in our experiments. As brain softenings were shown to be surrounded by a tissue zone with a pronounced disturbance of the vascular permeability (*Broman*, 1944), and in view of the fact that a marked vascular disorder was manifest in fresh and presumably primary necrotic areas caused by carbon monoxide intoxication (*Broman*, unpublished study), the second explanation seems to be most probable. The third explanation does, however, not seem to be at all unreasonable, even though no evidence in favour thereof could be produced except the observed excessive delicacy of the vessels.

The possibility of dural vessels being able to grow into a damaged area of the brain and thus give rise to a permanent disturbance in the vascular permeability in the cicatrized area could not be confirmed in the present investigation. But the investigation did not either show that this might not be the case, because in those few animals which were allowed to live sufficiently long after the damage to render such an examination possible the primary union between the dura and the brain ceased and was not substituted by permanent adhesions. As far as this question is concerned, our experiments were thus not able to show any clear evidence. In man it has been shown that if gross damages occur, such adherences some-

times arise, the dural tissues partaking in the formation of the cerebral scar, and the permanent occurrence in scars, of vessels without those permeability properties peculiar to normal cerebral vessels, may be of physiopathological importance.

SUMMARY

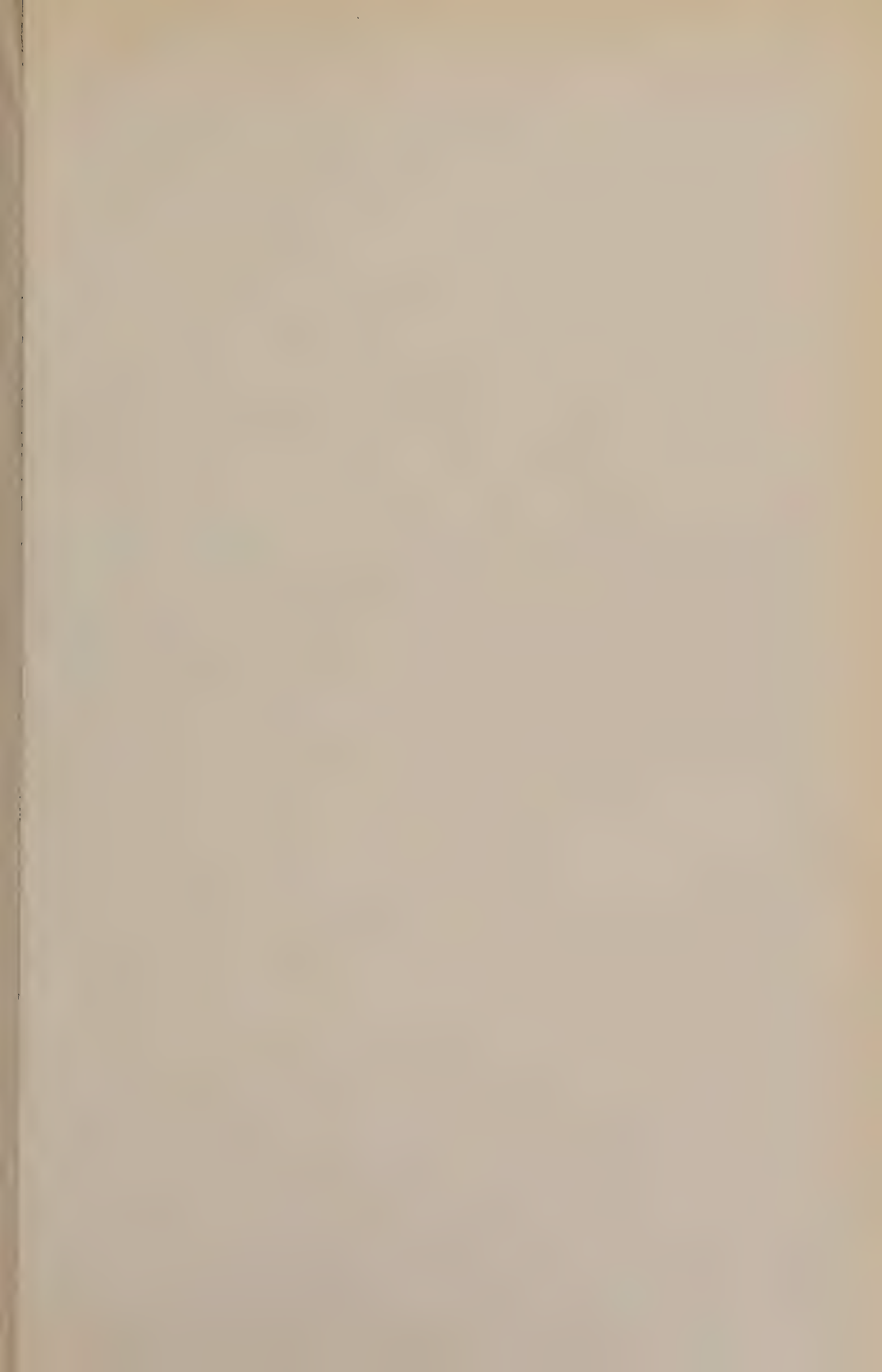
Relatively gross damage was produced experimentally by electrocoagulation in a circumscribed region of the brains of rabbits and cats. The purpose in view was to determine the duration of the disorder in the vascular permeability subsequent to such injury. It was found that in the beginning a pronounced disorder of the vascular permeability was demonstrable. Later, during the first day after the injury an increasing stasis arose in the vessels in the centre of the lesion so that finally the vessels contained no circulating blood. On the other hand, in the peripheral area of the damaged zone there were passable vessels which showed evidence of a disorder in their permeability lasting as long as one week subsequent to the damage. The reason why this disorder should last so long is discussed, and it is suggested that this persistence might be due to a toxic lesion ascribable to autolytic processes.

In the present investigation no dural vessels growing into the brain scar were demonstrable, but the existence of such vessels in certain gross cicatrical formations in man is a well-known fact that may be of physiopathologic importance not only mechanically but also from the point of view of permeability. If the experimental damage is infected so that abscesses develop, the perifocal disturbance in the vascular permeability will persist probably as long as the abscess lasts. In our experiments the disturbance in the permeability was limited to the thin capsule of the abscess.

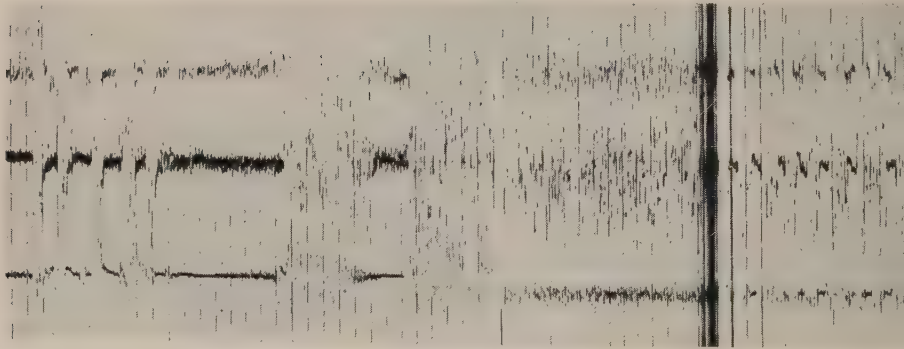
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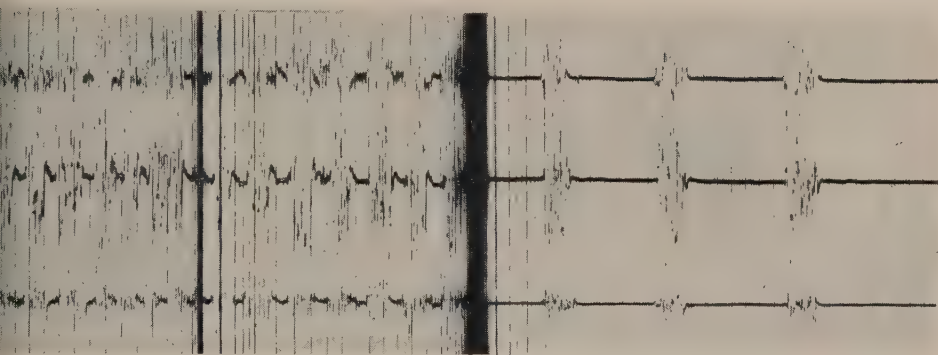


Metrazol seizure. Electromyographic
1 = triceps surae sin., 2 = t
Timing: thick and thin lines

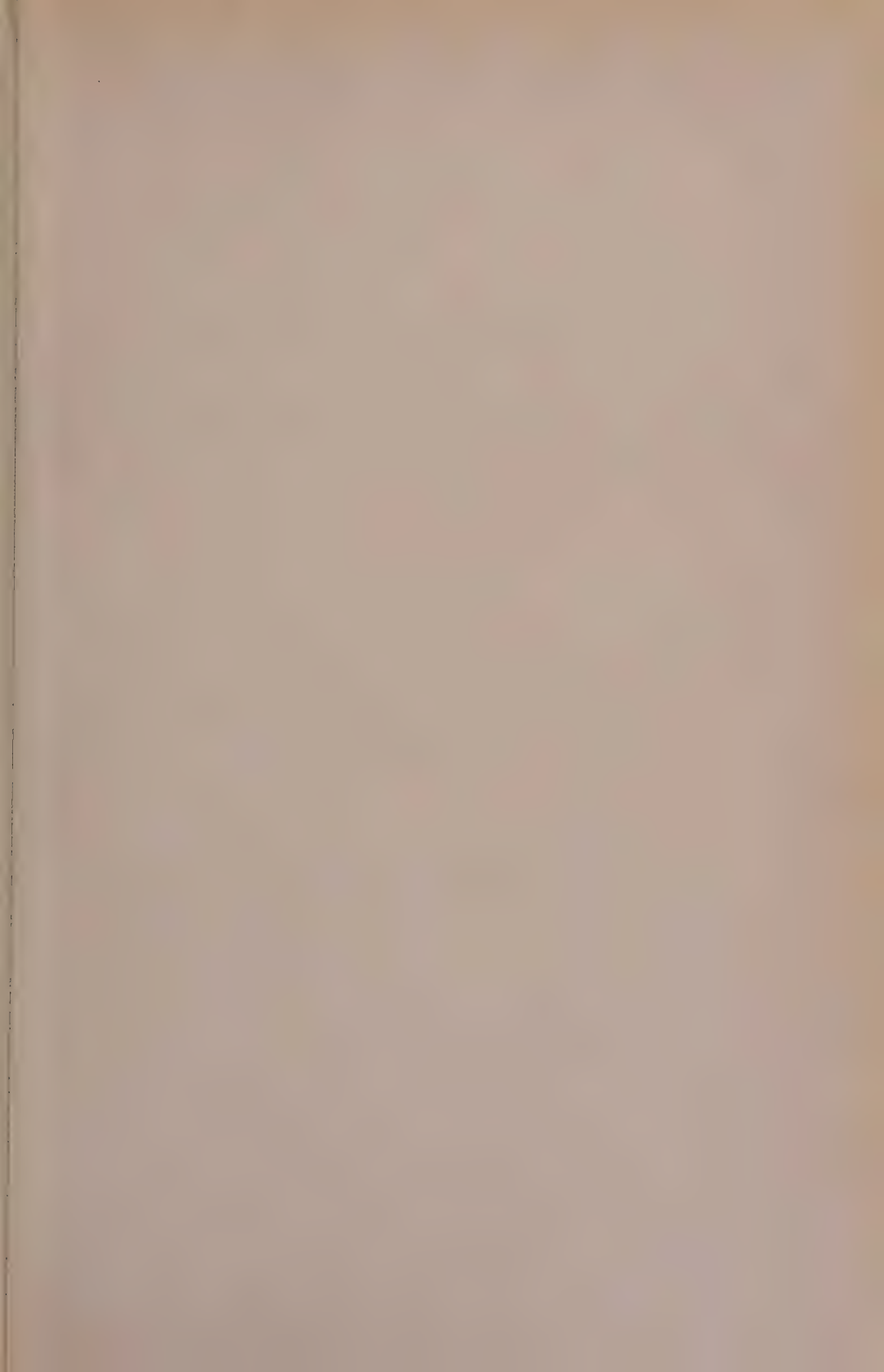


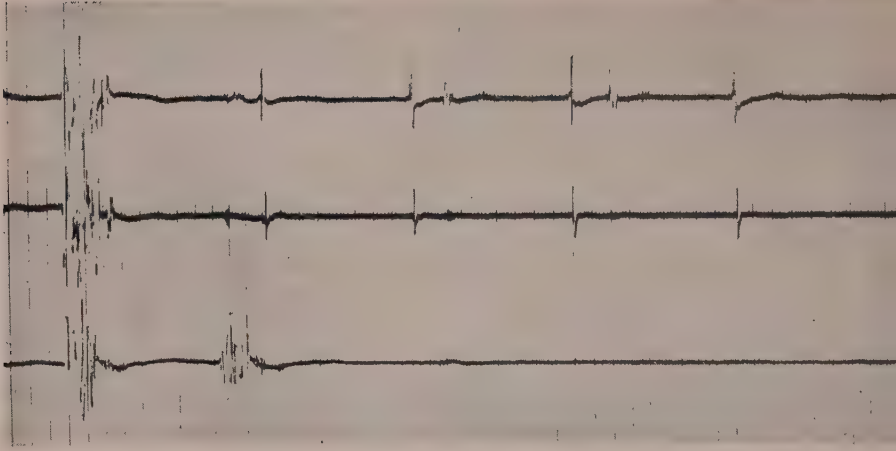
(a) first clonic phase, (b) tonic cramp, (c, d,

1.
stration with subcutaneous electrodes:
is ant. sin., 3 = triceps surae dx.
esponding to 10 cs and 2 cs resp.

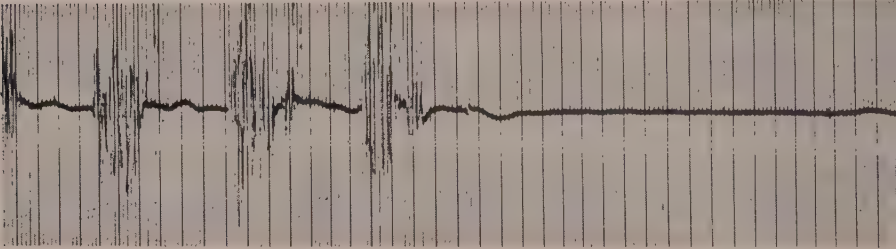


e) clonic convulsions with decreasing frequency.

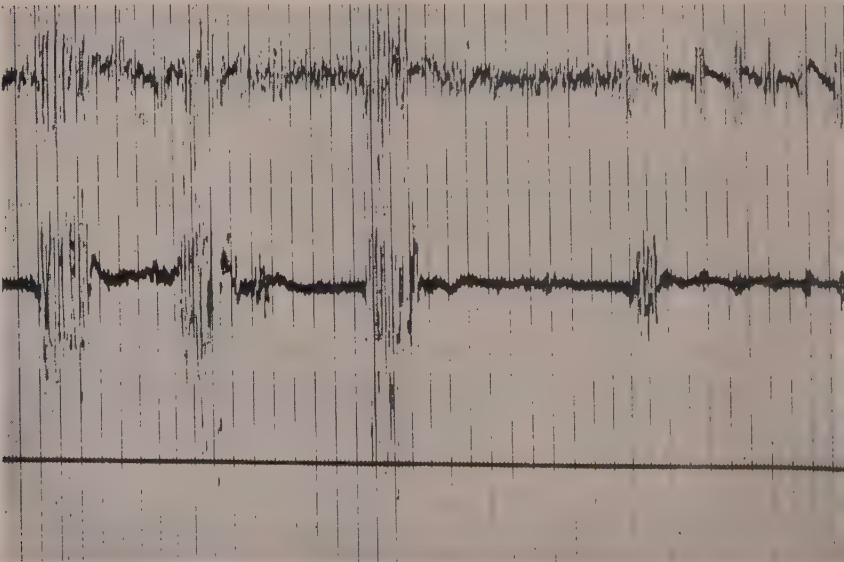




(a) Electro-shock seizure. Electrodes as in Fig. 1. A series of ankle jerks are seen. The convulsion is asymmetric.

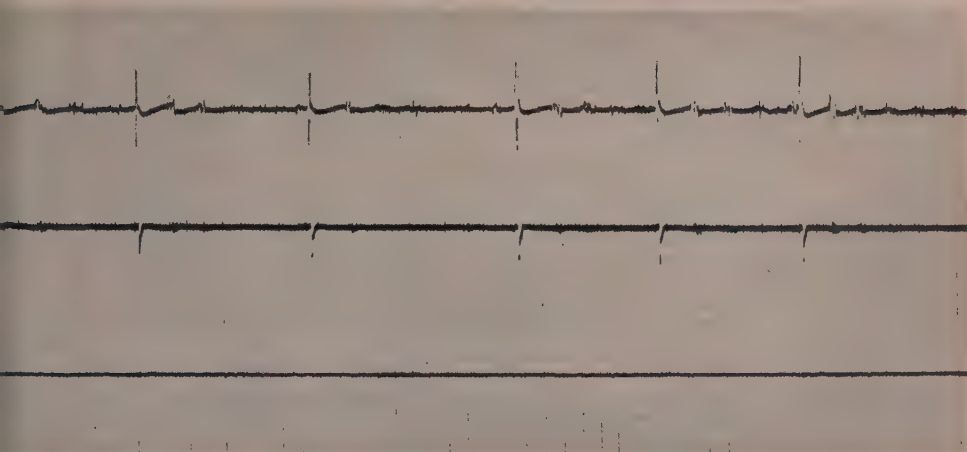


(b) Electro-shock seizure. Electrodes in the triceps surae sin. A s

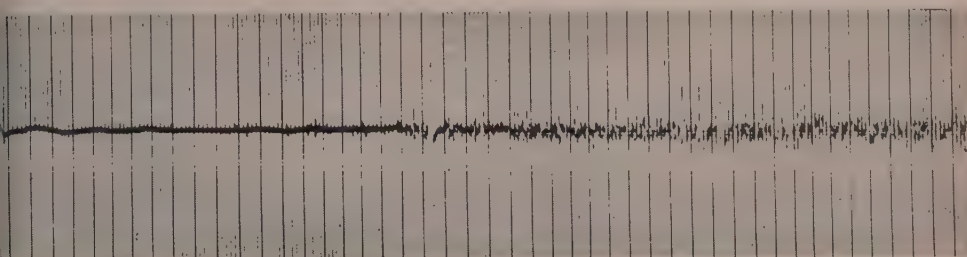


(c) Metrazol seizure. Electrodes 1 and 2 in the left
A spontaneous activity is seen the whole time between the last clonic con
flex.

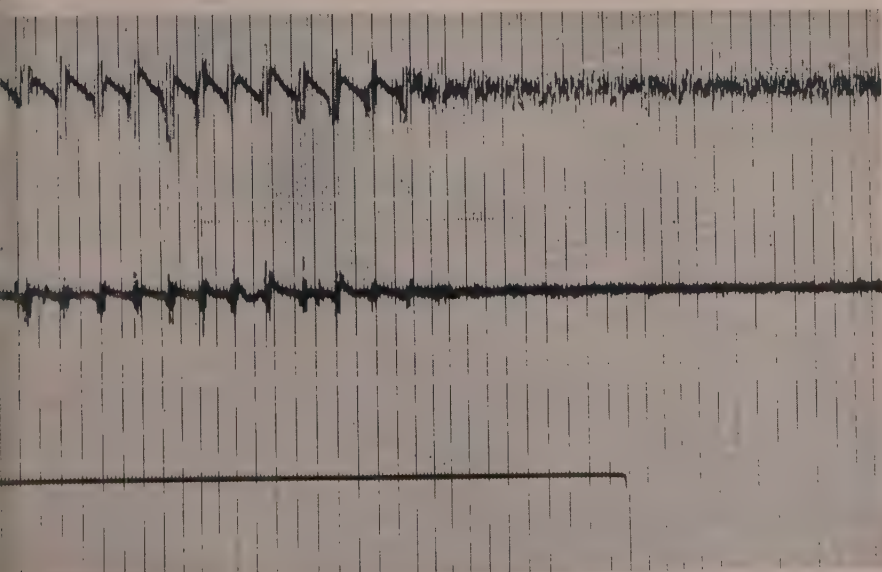
2.
c registration with subcutaneous electrodes.



elicted on the left side, showing an increasing tendency to clonus reaction. (The last
restricted to the right leg.)

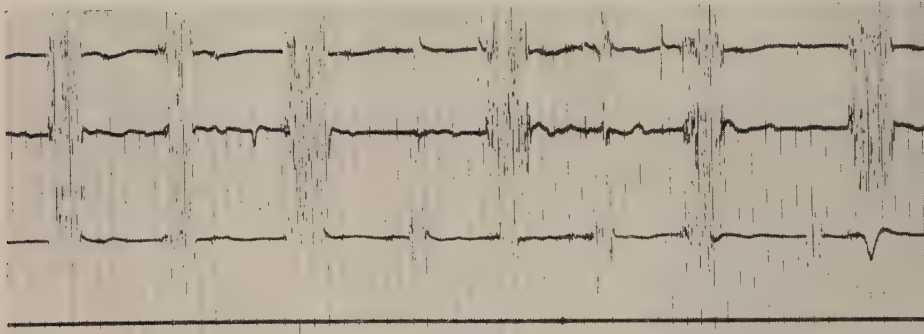


taneous activity appears already 4-5 seconds after the last convulsion.



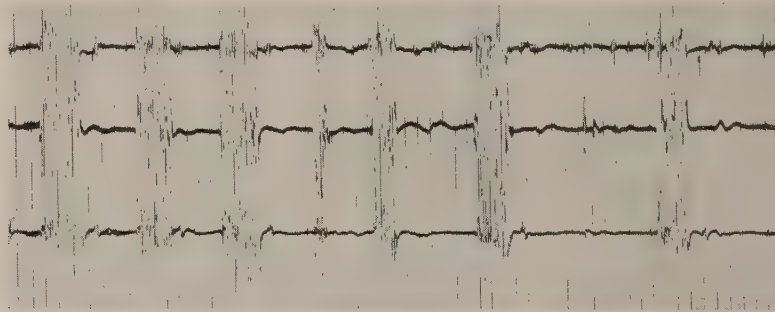
as in (a). 3 = signal indicating the starting of the breathing.
tions and after the end of the fit. An ankle clonus is easily elicited by a dorsal
of the foot↓.

Ankle jerks (and clonus) elicited *during* and immediately after the



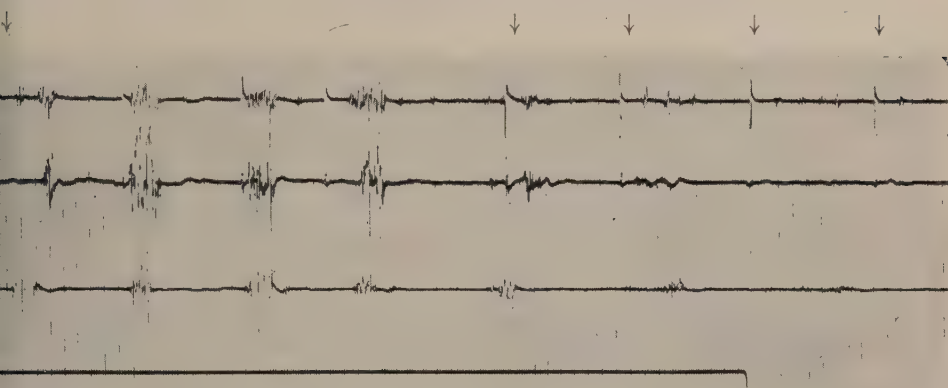
(a) Electro-shock seizure. The convulsions are partially asymmetric in time and (stimulated by the passive stretching of the M. triceps surae?). The br

↓

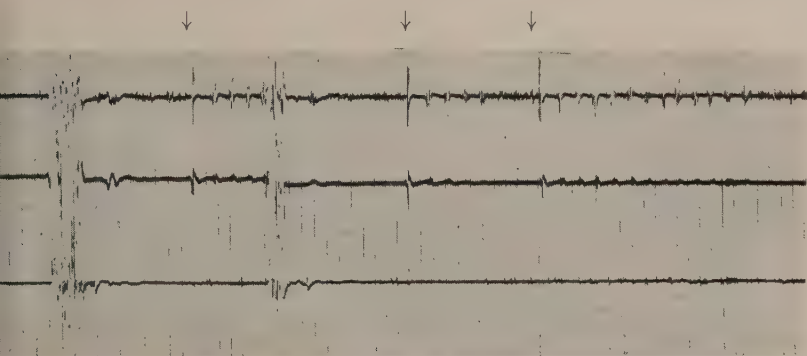


(b) Mertazol seizure. The increasing intervals between the last out of ce

3.
 st clonic stage of the seizure↓. Subcutaneous electrodes as in Fig. 1.



tion. Certain spike groups seem to have dropped out in the left leg but reappear later
 ng starts, as indicated by line 4, immediately after the last convulsion.



e contractions seem to be connected with a splitting up and dropping
 spike groups.

FROM THE PSYCHIATRIC CLINIC OF THE CAROLINE INSTITUTE,
STOCKHOLM. DIRECTOR: PROFESSOR T. SJÖGREN,
AND THE PATHOLOGICAL INSTITUTE, UPSALA, DIRECTOR:
PROFESSOR N. GELLERSTEDT

EXTENSIVE ENCEPHALOMALACIA AFTER TOXAEMIA OF PREGNANCY

BY

G. HOLMBERG

Despite the careful attention which has been devoted since the nineties to the pathological, patho-physiological, clinical, and therapeutic aspects of the toxæmias of pregnancy, we are not much nearer to a clear understanding of their nature than we were at the beginning of the century. Now that the pathologists have more or less completed the picture of the damage which these toxæmias can do to the body, attention is being paid principally to the physiological aspects in the attempts that are being made to clarify the condition. Clinicians have learnt to recognise the disease at an early stage and there is general agreement as to the overwhelming importance of prophylaxis in the fight against it. The therapy of the fully developed illness is also making some progress.

A common sign of toxæmia of pregnancy is the eclamptic attack, and in the past the disease did not come under treatment until it reached this serious stage. We have gradually learnt to recognise the "pre-eclamptic" stage, or "eclampsism", and have realised that the disease is frequently unaccompanied by convulsions, i.e. "eclampsia without convulsions".

In cases where eclamptic attacks occur, the cerebral features of the condition are very obvious, and therapy has been designed for a long time to check these cerebral manifestations by sedative treatment. Postmortem examination of patients

who have died in eclampsia has almost always revealed (Freund¹) some damage to the brain, usually in the form of diffuse or disseminated parenchymal damage, haemorrhages, or oedema.

Although cerebral symptoms have been observed from the first, and although cerebral damage (often insignificant but nevertheless incontrovertible) has commonly been found, very little attention seems to have been paid to the rôle played by the nervous system in toxæmias of pregnancy and it is surprising to note that many reports on eclamptic attacks do not state whether cerebral symptoms were observed or investigated by the clinicians or pathologists. This may be explained to some extent by the fact that signs of cerebral foci are often absent, have no time to develop, or are hard to discover since the patient is comatose during the whole course of the disease. Furthermore, many of the eclamptic cerebral disturbances of vision, aphasias, pareses, and other focal manifestations may be ephemeral or prognostically innocent. The view generally held by obstetricians is that eclamptic patients recover completely if they can only survive the critical days (Zweifel²). Dieckmann³ in his book on eclampsia (1942) states that there are probably more than 13,000 cases annually in the U.S.A.; 80-85 per cent of these patients survive the disease, and still there are no reports available on resultant pareses, psychological disturbances, or other signs of cerebral pathology. Dieckmann considers that other contributory factors were at work in a case of softening of the cerebral cortex described by de Vries.

One can, however, find several reports in the literature of severe cerebral damage which has been directly associated with toxæmia of pregnancy. Already in 1790, Amand⁴ is reported to have described a case in which there was permanent loss of the ability to read and write and mild dementia after eclampsia. According to Schmorl⁵, cerebral haemorrhages were very common before 1892 when treatment was expectant. Massive apoplexy was not uncommon at that time (see also Essen-Möller⁶). After the introduction of active therapy, the

main feature of which is the immediate delivery of the patient, the incidence of cerebral haemorrhage declined enormously.

The cerebral damage which has followed eclamptic attacks in recent times usually has not consisted of apoplectic haemorrhages but of small, disseminated lesions of the type described by v. Braunmühl⁷, Benoit⁸, Bodechtel⁹, and others. These lesions primarily consist of small foci of pallor and softening in various stages and small haemorrhages. Oedema and reactive changes in the glial tissue are usually found. Even these small lesions may, however, if they are very numerous and extensive, occasion a grave clinical picture. Nevermann¹⁰ reported (1927) that one of his 60 eclamptic cases when followed up had a residual right-sided hemianopia, slight disturbances of coordination and remnants of aphasia. A patient described by Liebers¹¹ was very taciturn after eclampsia, disorientated and suffering from slight paresis of the right arm. Postmortem examination revealed unusually severe and extensive lesions of the kind described. It should be noted that this patient did not die until the 13th day after the eclampsia. Diamond¹² has reported some similar cases, but he gives no details of neurological findings. Környey¹³ has carefully described a case in which the patient developed serious cerebral symptoms (after eclamptic convulsions) amounting to a decerebration syndrome, in which, however, irritation and deficiency phenomena from some different cortical areas could be distinguished. Numerous small foci were found closely scattered through the brain, particularly in the cortex. It is well-known that disturbances of vision often accompany eclampsia. These depend in part upon retinal phenomena, which can be directly observed as vascular spasm, etc., and in part upon cerebral pathology. So-called eclamptic amaurosis is believed to be partly functional in nature, and in any case the prognosis is usually excellent.

Other types of cerebral damage have also been described which impress one by their extensive nature. I wish to quote two such cases from the literature which are particularly surprising in extent and character.

One case was observed by Meltzer¹⁴; she was a 32-year old quinquipara who had had normal parturition, but ten days later was suddenly found one morning to be aphasic and paralysed on the right side. The provisional diagnosis was "post-partum cerebral embolus". The patient learnt to walk after 6 weeks, but the right side remained spastic and the motor aphasia did not clear up. She understood what was said to her and was able to give considerable help at the hospitals where she was subsequently a permanent inmate. When she died 15 years later it was found that the whole of the left front lobe had been absorbed, leaving nothing but the meninges. The corresponding pathways had undergone secondary atrophy and the basal ganglia on the same side had disappeared. The adjacent regions which had not become cystic had also undergone severe degeneration and it was particularly notable that the areas of degeneration were almost entirely limited to the subcortical zone, which was the seat of typical cerebral scar tissue. The left middle cerebral artery ran only a very short course before narrowing down and losing its lumen. The writer points out that this enormous cerebral damage must have been caused by one single episode and he expresses surprise that the patient survived without being seriously affected. It was considered that the postmortem excluded haemorrhage and thrombosis as the cause of the lesions, and since no conceivable source of substantial emboli could be found, the writer suggests air emboli as the probable cause. He observes that several cases have been reported in which air embolism occurred some days after parturition, particularly when the patients have lain in the knee-chest position.

The other case was an extensive atrophy of the brain in a 20-year old primipara, described by Lowenberg and Lossman¹⁵. Since 3 days before parturition, this patient suffered from headache, raised blood pressure and proteinuria. After a normal delivery, she went into severe convulsions which lasted 14 hours, and did not regain consciousness for four days. She gradually improved but remained demented, totally paralysed

and unable to speak. She continued this vegetative existence for 6 years. When she died the brain was found to be immensely atrophied; the writer considers that it had shrunk to about 40 per cent of its normal weight. The immediate original lesion had cut off practically the whole of the cortex from the lower centres and caused a veritable decerebration. The lesions on the whole were severer in the white matter than in the cortex, but they were mainly located in the border-line areas and included the deeper parts of the cortex. The most pronounced malacia was found in the frontal, temporal, and parietal lobes; the pre- and post-central convolutions and the occipital lobes were only moderately atrophied. The caudate, the putamen, and the pallidum were moderately atrophied and the whole thalamus severely so. The pons and cerebellum were also partially affected.—In the view of the writers, none of the known forms of eclamptic lesions could suffice to explain this immense destruction of brain tissue and they consider that it must have been a primary toxic effect. They quote for purposes of comparison a case of acute myocardial degeneration described by Ottow¹⁶ which was discovered after death from toxæmia of pregnancy.

Despite the difference in the site of the cerebral malacia, these two cases resemble each other in the extent of the malacia, which seems almost inexplicable when compared with the less disseminated foci of pallor and malacia of obvious vascular origin which have been present in most of the other known cases. As far as the case described by Meltzer is concerned, it is, however, possible that there may have been a venous thrombosis or some other lesion in a major vessel which could not be found 15 years later.

I wish to describe another case of widespread encephalomalacia in a pregnant woman, which I believe may have been due to a toxæmia of pregnancy¹.

¹ The notes in this case have been placed at my disposal by Professor T. Sjögren, Director at that time, and Docent B. J. Lindberg, the present Director of the Department of Mental Diseases of the Sahlgrenska Hospital, Gothenburg, where the patient was treated.

As the case was unusually well investigated and displays a number of interesting psychological, neurological, and morbid anatomical features, I shall quote the notes fairly extensively.

Mrs. F. E., 30 years (no. 405/40), was ambulant when she attended the Psychiatric Out-patients' Department with a relative. She had felt lonely and depressed since her husband had been called up for military service and when she visited her relative she was unwilling to talk. On examination, she appeared frightened, spoke very little and then in a low voice, could not remember how long she had been married or when her husband had left. She was admitted on the same day, 7/5 1940.

It transpired that she had always been delicate and neurasthenic, but had not previously been seriously ill. She had no children. For the next few days she was anxious and tense and slightly confused, and her reluctance to talk was particularly noticeable. She did not always reply when addressed, or said at most "yes" or "no", and never spoke spontaneously. Her behaviour and movements were also inhibited. She unbent after a few days and became more helpful and approachable. After 2-3 weeks, her inhibitions disappeared, but her speech remained very limited. Her memory also remained poor. She volunteered the information that she could neither speak, read, nor write. She said that her head felt queer and asked for it to be X-rayed. She denied that she had had headaches or convulsions and said she was no longer worried about anything in particular.

The physical examination on admission showed that her general condition was good. She was of leptosome build with normal covering. A short systolic blowing murmur could be heard at the base of the heart, which was otherwise normal. Blood pressure 140/115 mm Hg. The uterus was palpable one hand's breadth above the symphysis, corresponding to pregnancy in the 5th month. Neurological examination revealed a slight right low facial paresis but nothing else pathological. No dysarthria. Laboratory investigations: Blood — no an-

aemia, w. b. c. 8,000. E.S.R. 10 mm. Udine: No proteins or sugar, no deposit.

Gynaecological examination at the women's clinic elicited the following report "Normal pregnancy 5th month". X-ray of skull: N.A.D.

Even after some improvement had occurred it could be shown that the patient's memory and power to receive impressions were very defective and that she was easily mentally fatigued. She forgot almost at once what was said to her. For a time she was difficult, obstinate, and absurd in her behaviour without, however, displaying any sign of schizophrenia. Besides her difficulty in speaking, she had a slight tendency towards unwarranted laughter suggesting obsessional laughter or embarrassment. Her expression was always contented and unmoved, and lacked the normal emotional changes. There were also signs of euphoria and insensitivity. When she was advised to take up some handwork she complained that she could not read or sew because she "saw double". There was no true diplopia.

The patient stated that she had found school, and in particular arithmetic, difficult. Various tests were applied to her. By the Point Scale and Wåhlén methods (values corrected according to Lindberg) she was found to have a mental age of 12 years. The Bourdon and Ebbinghaus tests showed that she had great difficulty in concentrating, was slow and inattentive. The examiner found that she had great difficulty in expressing herself. Every letter had to be written for her because she said she had forgotten what the letters looked like. She had not, however, completely lost her visual "Gestalt" functions since she could draw ordinary objects (in point scale) fairly well and remember them to some extent.

She improved slowly for a couple of months and began to feel well though rather tired. She worked every day in the weaving room and gave a hand in the ward. Only her facial paresis seemed to get worse. Otherwise there was nothing abnormal in her nervous system. She became more and more active and even displayed a certain amount of initiative on

occasion. On the 18.7 was recorded: "Very little psycho-pathology can now be observed".—The facial paresis, which was thought to be cerebral in origin, varied noticeably in a matter of days and appeared now to be less pronounced.

Routine urine examination on the 25.7 yielded positive Heller and a few r.b.c. and organisms in the sediment. On the 29.7 proteins were still present. On the 31.7, when blood was being taken for a blood urea estimation, the patient suddenly went stiff in the right half of her face and the angle of the mouth on that side was drawn across. At the same time she became again quiet, reserved, and obtuse. For a brief moment she was angry and desperate, struck a nurse and tried to run away. Then she became stiff in body and face.—After this episode she seemed slightly confused, and answered in monosyllables or not at all when addressed. Apart from the facial paresis there was nothing abnormal to be found at neurological investigation.

On the day after, the 1.8, the right-sided facial paresis was less pronounced but still obvious. No new neurological signs were found. The patient, who seemed stiff and reserved, complained of a headache, which she said she had had for some time. The pain was situated in the frontal and occipital regions and around the left ear. Together with the headache, she had giddiness and a feeling of faintness; sometimes she retched. No foetal movements had been observed since the 1.8.

It was suspected that she was suffering from a toxæmia of pregnancy and she was sent with this label *to the gynaecological out-patients' department and to the ear department for special investigation*. The otologist found nothing abnormal. The gynaecologist thought that the foetus might have died but found no sign of toxæmia of pregnancy. He suggested that she be examined again two weeks later.

On the 7.8 there was still a trace of protein in the urine. The facial paresis was less pronounced. Apart from her rather stiff gait, her expressionless face and hypokinesia she had nothing abnormal in her nervous system. She lacked initiative, was quite passive and only answered "yes" or "no" when

addressed. She improved so much, however, that she was soon able to manage her own toilet. Her appetite was poor and she began to lose weight on the 12.8.

On the 17.8 the patient was referred to the women's clinic and she was admitted to the obstetric department on the 20.8. The notes from that department record that she lay still in bed with a mask-like expression on her face constantly repeating single words. No foetal sounds were heard. A few leucocytes in the urine but nothing else abnormal. On the 21.8 towards evening the patient became restless, but it was not certain whether she was in pain and she was given a sleeping draught. During the night a macerated foetus was produced.

On the 24.8 the patient returned to the psychiatric department. She was in stupor and did not reply when addressed. Her head was twisted to the right—a new development. She found it hard to swallow liquids and she was incontinent of urine.

On the 25.8 a distinct conjugate deviation to the right was observed. The patient was still stuporous but responded sometimes when spoken to with perseveration or *ekolalia*. The left pupil was not quite circular and slightly larger than the right. Occasionally there was nystagmus to the right. Fundi: nothing to be seen for certain. A clear left lower facial paresis was now seen and the left side of the palate was lower than the right. There was extreme spasticity in all the muscles of the extremities; the legs were held straight, the arms bent and pressed to the side of the body with the hands in tetanic position. On the right side this spasticity was constant, but on the left it varied from hour to hour. Abdominal reflexes normal. Babinski negative both sides.—Towards evening the temperature rose to 38.6° C. Blood urea 31 mg%. Blood sugar 0.07 per cent.

For the next few days the patient had marked rigidity in the neck muscles and conjugate deviation to the right together with spasticity in the right arm and leg. On the left side there was varying hypertonus and spastic phenomena and occasionally complete paresis. The facial paresis was now

bilateral but most marked on the left. Sensation doubtful on the left side of the face. Left pupil slightly enlarged and reacting sluggishly to light. Speech disarticulate and slurred with a pronounced tendency to perseveration. The patient did not generally respond when addressed. She fell into a delirium-like condition with constant spontaneous monoverbal perseveration.

An eye specialist was summoned. There were no choked discs nor other pathological lesions in the fundi. *Lumbar puncture* on the 26.8: pressure 150 mm. of water, clear fluid, Queckenstedt neg., Nonne (+), protein 22 mg.%, Pandy +, cells — 1 polymorph per 3.2 cu. mm. Mastix — no flocculation. All lues tests negative.—Blood calcium 9.8 mg.%, control 10.6.

On the 27.8 the patient also had choreiform movements in the right hand which was slightly acrocyanotic. She understood questions and could give simple answers, but perseveration continued. When asked her name she mumbled "Ekstrand, Ekstrand, Ekstrand ..." and she stated her age, address, and date of birth in the same way. When asked to put out her tongue she perseverated the request but did not perform the movement. When she was asked to greet the doctor she said: "Good morning doctor, good morning doctor ..." but did not extend her hand. She had demonstrable slight amnesic aphasia with paraphasia and verbal perseveration.—The urine contained proteins and a moderate amount of white blood corpuscles. E.S.R. 52 mm.

On the next day the patient was worse. She was drowsier, lay for hours perseverating single words at a rapid rate in a monotonous voice and with poor articulation. The spasticity in the left arm had increased. Trömmer reflex bilaterally positive. Abdominal reflexes absent on the left, present on the right. Babinski negative on the left; violent withdrawal on the right.—On the following day articulation had deteriorated still further and there was difficulty in swallowing. Some spontaneous movements were observed in the right arm and leg

but the left side was immobile. The fingers of both hands were very tense so that the Trömmer reflex could not be tested. The right patellar reflex was very much increased, and the left slightly so. Babinski negative both sides.—The blood contained increased amount of neutrophils (12,000 leucocytes) and an increase in the number of rod cells (28 per cent). Myelocytes 0.5 per cent.

The patient's condition remained more or less unchanged during the next few days. Ekolalia and perseveration continued. The patient reacted slightly to pinpricks and withdrew the left knee when pricked on the legs. Bracho-radialis reflexes very much increased, more so on the left. Babinski bilaterally negative. — 2.9. Urine: Heller +. Centrifuged deposit (catheter specimen) contained a moderate number of leucocytes. Blood: E.S.R. 69 mm. Blood sugar 0.12 per cent.

19.9.—*Ophthalmic examination*. Pupils and fundi N.A.D. 21.9 — *Lumbar puncture*. N.A.D. 23.9 — Urine: Heller +, deposit contained a number of white blood corpuscles.

24.9: patient did not react to any stimuli. Incapable of visual fixation. She could not eat and was given nourishment by enema. Incontinence of urine and faeces.—The spasticity on the right side and the left hemiplegia and hemi-anaesthesia remained. Ketonuria.

27.9: Ketonuria, glycosuria, proteinuria, occasional white cells in the urine. 1.10: Numerous r.b.c. in urine as well. 2.10: Blood urea 43 mg.%. 4.10: Very numerous white cells and bacteria and a few r.b.c. in urine.

From then on the patient was stuporous, but occasionally seemed to react emotionally. On the 9.10 her eyes filled with tears when she was given a message from her husband. The left facial palsy seemed to be spreading to the frontalis muscle (but there was no lagophthalmus or ptosis). For the rest, neurological examination revealed nothing new.

She deteriorated physically. The urinary infection persisted. No change in nervous system. On the 25.10 she became suddenly worse and went into coma.

DEATH OCCURRED ON THE 27.10

Postmortem on the 28.10 (Dr. Gert Vejlens).

Pathological diagnosis: Cerebral softening and degeneration of the liver parenchyma.

The brain substance was pale throughout. Numerous pale grey-white areas of softening varying from the size of a pepper corn to that of a plum were seen in both hemispheres, particularly on the right and mainly at the border between the cortex and the grey matter in the parietal and temporal lobes. No macroscopic lesions in the sinuses or arteries of the brain.

Heart rather small and firm. Valves and coronary vessels normal. Musculature pale brown. Lungs filled with air throughout. Spleen rather large and doughy. Cut surface pale yellow-brown. Structure invisible. Kidneys of normal size and pale. Pattern distinct. Pelvic organs normal.

Histological examination. The liver has undergone intense parenchymatous degeneration, with fatty change. Its appearance is compatible with a toxæmia of pregnancy.

Pathological diagnosis: Subacute interstitial glomerulonephritis and nephosis.

Investigation at the Brain Laboratory, the Pathological Institute, Upsala, by Professor N. Gellerstedt the 18th December 1940.

Formalin-fixed brain. Neuropathological diagnosis: Bilateral encephalomalacia.

Orientation and reconstruction were difficult because the brain was so cut to pieces that the distribution of the foci could not be precisely determined. The brain contains not more than three macroscopic foci of old pure malacia with severe vascular and glial reaction. Microscopically, however, the process is far more extensive than could have been envisaged macroscopically. Thus pre-malacial areas can be seen, as well as glial "Abbau" at several points in the central ganglia (especially in the dorso-medial thalamus, the internal capsule and the inferior colliculi). Severe secondary descend-

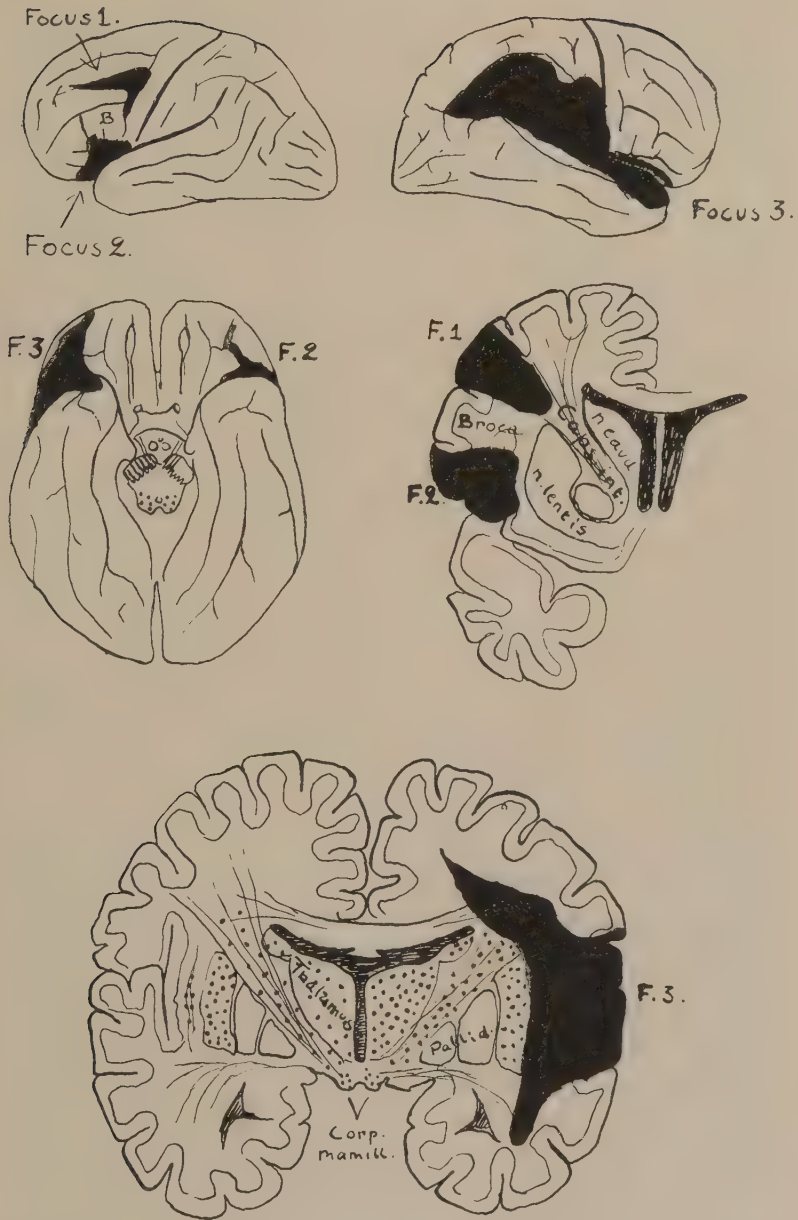


Fig. 1.

Fig. showing the distribution of cerebral lesions. There are three massive foci, scattered small foci and secondary degeneration (in the peduncles).

ing degeneration in the right peduncle and in the medial third of the left peduncle. Also severe gliosis and total loss of nerve cells bilaterally in the dorsal portion of the inferior olivary nuclei. The other nuclei of the medulla oblongata (and the other cranial nerve nuclei) are not affected.

The position and distribution of the large areas of softening are seen in the attached figures. Focus 1 does not extend into Broca's convolution, but involves part of the motor centre for head and eye movements and affects the front lateral part of the internal capsule (= partial degeneration in the left peduncle). Focus 2 lies mainly below Broca's convolution and extends to the base of the frontal lobe. The large focus 3 stretches back to the edge of the occipital lobe, across the angular gyrus and the supramarginal gyrus, along the superior temporal gyrus to the tip of the temporal lobe and thence across to the lateral part of the base of the frontal lobe. Within, it affects mainly the opercular regions opposite the insula, as well as the latter itself. In front of and behind this "centre" the focus extends like a sagittal column just lateral to the lenticular nucleus and cuts off practically the whole of the radiation of the internal capsule. One can safely say, therefore, that almost the whole of the cerebral cortex is cut off from the brain stem.

If the patient was left-handed it would be easy to explain her speech defect, but difficult if she was right-handed since the auditory and visual speech centres on the left side are not destroyed. Broca's area is touched on both sides but the records do not state that the patient was dumb. The various cranial nerve symptoms were doubtless cortical: the foci touch the lowest part of the central convolution on each side. The conjugate deviation can be explained by Focus 1, unless it was due to the large focus on the other side. The spasticity on the right is hard to explain: possibly it is due in some measure to the bilateral lesions in the thalamus and in the mesencephalon.

The cause of the malacia cannot be determined histologic-

ally. It is certain, however, that there is no vascular lesion (arteriosclerosis, inflammation, etc.). No thrombi or remnants thereof were found. *Probably* the process began with small emboli, as the general nature of the foci suggests (n.b. acrocyanosis in the right hand). There may have been spasm in various arterial fields, and this would explain the progressive nature of the condition. It is certainly nothing but a disturbance of vascular function. I do not think it is a toxæmia of pregnancy. The liver and kidneys do not show the lesions characteristic of that condition.

COMMENTARY

The patient was a 30-year old woman who on arrival in hospital showed signs of depression and inhibition. She was in the fifth month of pregnancy. The disease gave the impression of a psychogenic depression in a pregnant woman.

The patient's general condition was good. Blood pressure 140/115 mgHg, which is high and cannot be regarded as fully normal (see Dieckmann³). A moderate leucocytosis is a feature of pregnancy. Blood and urine tests otherwise normal. Neurological examination revealed a slight right-sided lower facial paresis. The obstetrician stated that the case showed no sign of complications.

When her psychological inhibition disappeared after a short time, difficulty in speaking, writing, and reading remained. Defects in vision occurred as well. The power to receive and retain impressions was so poor that she suggested a Korsakow syndrome. Her behaviour was stiff and awkward and there was a hint of obsessional laughter. Facial expression contented and unmoved. The patient may have been a little euphoric and emotionally blunted.

These symptoms were rather diffuse both in themselves and because they could not be attributed to any localised brain defect. On the whole the patient's behaviour was reminiscent of a pre-catatonic condition. It may be taken for

certain that true "dysphasia", "dysgraphia" and "dyslexia" were present and there were probably also defects in visual interpretation. If one adds to this a Korsakow-like amnesic syndrome, it is clear that scarcely any part of the brain had been unaffected, or at least that the greater part of the left hemisphere was involved. The slight right-sided facial paresis of a central type confirms this lesion. It is therefore evident that the patient, when she arrived at hospital, had extensive lesions in her brain. Judging from the course of the illness, however, these changes were in part reversible. (See *inter alia* Spielmeyer¹⁷). The inhibition and other symptoms became less marked. Facial paresis, on the other hand, seemed to grow worse, which may signify that a localised irreversible cerebral lesion had developed.

It is not known how this first syndrome arose. Laboratory tests and somatic findings on admission provide no clue to the aetiology. The subsequent history of the disease gives a clear indication, however, of its nature. *Routine tests revealed the development of proteinuria and a pathological deposit, and it was in association with these findings that a new set of symptoms were observed.* The precipitating cause was a painful venipuncture. An episode that was almost catatonic introduced the exacerbation and the facial paresis became noticeably worse. The stage of stupor was only a short one, but the patient then complained that she had had a headache for some time. No foetal movements were observed after this exacerbation.

This suggests a toxæmia of pregnancy, and the patient was referred to the women's clinic with this diagnosis. Although no further signs were found to confirm this diagnosis there is little reason to doubt that it was correct. Pregnancy had reached the eighth month. It is true that no convulsions had occurred and that very little was found in the urine—but neither feature necessarily occurs in eclampsia. (See Elis Essen-Möller⁶). A symptom which is almost essential to the picture is arterial hypertension, and this was in fact present on admission. It is to be regretted that continuous blood

pressure readings are not to be found in the otherwise very exhaustive notes of the case¹.

(Rises in blood pressure may also be transient and are not always discovered.)

The headache was located particularly in the region of the left ear. Nothing abnormal was found by the otologist. This may suggest that the diseased process took place mainly in the left half of the brain.

After the exacerbation, the patient's condition was worse than it had been before; she was drowsy, lacked initiative, spoke very little and moved unwillingly. She began to lose weight.

A couple of weeks later she was transferred to the obstetric department where she delivered a foetus which seemed to have been dead for some time. The day before parturition, she lay still with a mask-like face constantly repeating single words. White cells but no proteins were found in the urine. When she returned to the psychiatric department she was found to have developed another phase of the illness, and the clinical picture was now very extensive. She was stuporous, had difficulty in swallowing and was incontinent of urine. Conjugate deviation and nystagmus to the right were observed and there was rigidity of the neck musculature and spasticity—not unlike decerebrate rigidity—in all the muscles of the extremities. An obvious upper motor neuron facial paresis had developed on the left and the left palate was lower than the right. Besides the signs of widespread damage, therefore, there was also localising symptoms, of which the most pronounced was the conjugate deviation. There were also occasional choreiform movements of the right hand, which was the seat of mild acrocyanosis. Speech was reduced to a minimum, but the patient clearly understood part of what was said to her.

¹ The assistant physician, Dr. Greta Tessing, has informed me that the blood pressure was measured repeatedly, but the record seems to have been mislaid. Dr. Tessing remembers that a minor rise occurred in association with the exacerbations, but only one of about 5-10 mm Hg.

Her reactions suggested that there was some apraxia, but it is not impossible that these phenomena could be explained by her stuporous general condition. She had amnesic aphasia, paraphasia, and verbal perseveration.

The fact that this was a true toxæmia of pregnancy is confirmed by the decisive turn for the worse which accompanied parturition. Even immediately after it, proteins and white cells were found in the urine. The E.S.R. was high and reached its peak 12 days after parturition. There was also leucocytosis and a shift to the left—indicating that the bone marrow was affected. A difference soon became apparent between the extremities of the right and left sides; there was constant hypertonus in the right arm and leg, whereas the left varied so much that they were sometimes quite flaccid. The left arm and leg were spastic and paretic at a time when the limbs on the right were fairly strong and there was left-sided hemianaesthesia. Paresis of the left side of the face and palate was also present. The left pupil was enlarged and sluggish. There were definite signs of a left pyramidal tract lesion but not of a right one. (The bilateral facial paresis suggests, however, that there was a similar though smaller lesion on the right.)

This may be a suitable point at which to compare the clinical findings with the pathological ones. It is probable that the lesions in the central ganglia caused a general raising of muscle tonus. The difference in tonus on the right and left and the fact that choreiform movements appeared on the right but not on the left can be fully explained by the complete destruction of the tracts leading down to the left side. (See Meltzer and others.) For the rest, I would refer to the report of the brain pathologist, which gives a very probable explanation of the various phenomena. It is too difficult to consider the aphasic disturbances in detail and to attempt to correlate them with the distribution of the malacia, especially in view of the small foci which were disseminated throughout the brain and which may have affected speech. The rôle of the right hemisphere in these functions has been discussed and

it is probable that the central parts of the brain also play some part in speech. (Goldstein, Ustvedt¹⁸). Finally, death must have been due to the general deterioration in the patient's condition which followed the lesions in the brain and the internal organs. The urinary infection may have been another cause.

The histological picture can be divided into large focal lesions and smaller disseminated ones. All these lesions appear to have been of purely vascular origin. The small foci were apparently of the same type as those usually found in eclamptic cases but exceptionally widespread. It must be noted, however, that these lesions are not very specific, judging by the findings of Spielmeyer¹⁷. Lesions of this kind may be found in intoxications of various kinds, after multiple small emboli or thromboses, hypertensive crises, and other vasomotor disturbances in the brain which are difficult to explain but may have some mental basis.

As mentioned above, the aetiology in this case must be assumed to be the pathological process usually called toxæmia of pregnancy. The clinical course makes this diagnosis very probable. The absence of convulsions does not in any way contradict this diagnosis; it is rather the rule in cases where there is a really large cerebral lesion. This has been emphasised by Schwanen¹⁹ and others. Furthermore, distinct lesions were present in the liver and kidneys, although there is a difference of opinion as to their cause. In fact, none of the pathological findings oppose the diagnosis Toxaemia of Pregnancy and the reason for their somewhat ambiguous nature may well be that the patient lived so long that they changed their appearance.

DISCUSSION

The cerebral pathology associated with toxæmia of pregnancy is still far from clear. Braunmühl and Benoit have assumed that vasomotor disturbances in the smaller vessels play the main rôle and this seems to be supported by Spiel-

meyer's investigations. v. Braunmühl does not, however, exclude the possibility of toxic effects on the perivascular tissues. Spielmeyer advises the greatest care when drawing any conclusions from the appearance of the foci, for he considers that the most diverse train of events may end in the same patho-physiological events and the same tissue lesions. He is referring to cerebral vascular spasms and the ischaemic foci which they may cause.

As far as the toxin theory is concerned, the investigations of Broman and Broman²⁰ into the permeability of the cerebral vessels are worthy of mention. Broman has pointed out that a blood-borne protein antigen cannot induce local allergic reactions in the brain unless there is some damage to the vessel wall which permits the antigen to pass out from the blood into the brain tissue. Several toxic substances, including a couple of proteins, have been shown to be capable of damaging the vessel endothelium so that the same substance, or the blood plasma, can pass through and continue to exert its harmful action on the surrounding brain tissue, mainly by causing oedema. Histamine, which has been thought by many workers to play a part in eclamptic phenomena, has been found by experiment not to induce any such effect. Nevertheless one cannot ignore the rôle of histamine in vasomotor phenomena in the brain as elsewhere.

Most workers have agreed that spasm in the small vessels is one of the most important mechanisms in the occurrence of eclamptic cerebral lesions. It is not yet known what substances cause this spasm and the subsequent dilatation. It has been assumed that they are the same substances that raise the arterial blood pressure. For large areas of softening to result, either the small foci must lie very close to one another or the spasm must occur in large vessels as well as small. Changes in permeability with resulting oedema have been mentioned as important factors. This matter has not, however, been elucidated and it is not, therefore, known whether the large foci are caused by a process essentially different from that which causes the small ones.

In the case described in the foregoing, areas of softening were found of a completely different order of magnitude from that usual in eclamptic lesions. Their genesis deserves special discussion. Lowenberg and Lossman have felt compelled to resort to the toxin theory to explain their case. They consider that toxic effects of various kinds often occur particularly in the border between the grey and white matter, as in their case. Meltzer, who could find no case comparable to his own in the literature, proposed to attribute the immense damage he observed to air emboli. There does not appear to me to be any justification for this hypothesis. Neither the knee-chest nor the raised pelvis positions had been adopted and no operation had been performed. According to H. Fredriksson²¹, some adverse factor must be present for air emboli to occur. A patent foramen ovale is also necessary at least for the passage of large air emboli to the brain.

In my opinion, the cerebral damage in the case described by Lowenberg and Lossman, and possibly also in Meltzer's case, was of the same nature as that which I have described. The fact that in Meltzer's case the disease did not manifest itself until 10 days after parturition does not exclude this opinion since eclampsia occurring as late as this has already been described in the literature. In one case of Diamond's eclampsia appeared 9 days after parturition. (At postmortem, the placenta was found in the uterus.) A striking feature of all three cases is the localisation of the lesions in the sub-cortical zone. Probably there was a leakage of toxins into parts of the brain tissue where the vascular endothelium had been particularly damaged by these same toxins. Perivascular oedema of similar aetiology may also have had a deleterious effect. Judging from the clinical course, the brain lesions occurred sporadically.

The cases of encephalopathy after burns which have been described by Kruse²², Globus and Bender²³, L. Bender²⁴ and others are in certain respects comparable to the more severe postecclamptic encephalopathies. The clinical and pathological similarities between these two categories of brain damage

are so numerous that one can assume that they have occurred in a similar way. Convulsions and/or coma sometimes follow burns, appearing suddenly after an interval without any such manifestations. After an episode of the kind, neurological symptoms, aphasia, blindness, dementia, etc., may occur and the general condition of the patient may become critical. In one case, which ended fatally, (Globus and Bender) small disseminated foci of softening and (particularly in the sub-cortical region) glioses were found in the brain, very similar to some of the above-mentioned eclampsias^{11, 12, 13}.

The question then arises why extensive cerebral damage after toxæmia of pregnancy is not commoner or better known. The simplest explanation would be that patients in whom such severe lesions have developed usually die before the damage can be observed. Meltzer's case had lived 15 years after the damage was done. Lowenberg and Lossman's patient lived for 6 years, and the case I have described lived for over 2 months. Liebner and Környey's patients lived for 13 and 9 days, respectively, after the decisive catastrophes occurred, and there seems to be no doubt that the cerebral lesions in these two cases occupy an intermediate position between the three cases mentioned above and the vast majority of cases in which the patients have died soon after their eclamptic attack.—It seems then that once a patient has survived severe and widespread eclamptic cerebral damage, the duration of her subsequent life to some extent determines the development of the malacia.

Really widespread cerebral malacia is of course irreversible, but this does not seem to be true of the smallest lesions (cf. Spielmeyer.) In the case described, there were probably three bouts of the disease at fairly long intervals, between which the patient underwent a fair degree of recovery. It is probable that the improvement in symptoms can be attributed to the disappearance of cerebral oedema.

I have quoted some examples to show that severe brain damage after toxæmia of pregnancy is not as unusual as is generally imagined and that it may in some cases assume

enormous proportions. As Meltzer said in his paper it is surprising that his patient did not die immediately, and it is doubtless the case that widespread brain damage of this kind usually causes death so rapidly that it is never discovered either clinically or pathologically. Furthermore, it has not been the custom at all obstetric clinics to carry out a careful neurological examination on every case of eclampsia or a post-mortem examination of the brain in fatal cases. Schwanen is doubtless right when he says that the brain lesions which can be observed in nearly every case of eclampsia would be found to manifest themselves clinically in many more patients than they do if the neurological examination of eclamptic cases became the rule. Mental symptoms are also of interest, as for instance the catatonic phenomena which often occur. It is open to question whether the significance of the nervous system in the prognosis of severe eclampsia should not receive more attention. It is certainly unwarranted to assume that post-eclamptic cerebral damage is always insignificant or innocent.

S U M M A R Y

The writer describes two cases from the literature and a case of his own of widespread encephalomalacia attributed to toxæmia of pregnancy. He also quotes some cases of eclamptic brain lesions in which the damage was extensive, but large areas of softening had not had time to develop. These cases seem to provide a natural transition from the most severe type of case to the usual, mild, and apparently reversible type of eclamptic brain lesions.

Severe brain damage after toxæmia of pregnancy has been reported comparatively rarely and is quite unknown to many doctors. Neurological examination of all cases of eclampsia and an examination of the brain in all fatal cases should be a universal rule.

The genesis of the lesions is not fully understood, but the main factors are probably a vasomotor one, involving ischæ-

mia, and toxic damage to the vascular endothelium. Parenchymal damage may have been due to a direct toxic effect or a secondary consequence of the oedema of the brain.

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A TECHNICAL ERROR IN ELECTRO- MYOGRAPHY

BY

ARNE LUNDERVOLD

Electromyographic examination has now advanced so far that in some hospitals it is included among the ordinary methods of clinical examination. In suitable cases it may be of service both for diagnostic and prognostic purposes. One of the most important points on which the electromyogram gives information is the question whether synchronous motor units are present or not. In order to investigate this matter leads must be taken from several different places at the same time by means of an electromyograph having several separate channels (amplifiers).

Using this technique the Danish investigators Buchthal and Clemmesen in 1943 showed that such synchronisation of motor units is usually seen in poliomyelitis, amyotrophic lateral sclerosis and spinal muscular atrophy, *i.e.* in diseases presumably due to an affection of the anterior horn cells, while they do not find this synchronisation in more peripheral affections of the nerves. This finding they made on leading off simultaneously through several electrodes from the same muscle. The Norwegian investigator Birger Kaada, in a hitherto unpublished work, has recorded the same synchronisation in monkeys, inoculated with poliomyelitis virus. In healthy monkeys, on the other hand, he gets either single motor units or, on more vigorous contraction, an interference curve of the

same form as in human subjects. The American authors Watkins, Brazier and Schwab (1943) on leading off from several different muscles, for example from antagonists, have also found the same synchronisation of motor units in poliomyelitis, but in contrast to the Danish authors they find exactly the same electromyographic pictures in more peripheral nervous disorders, for instance in case of damaged nerves. But they do not mention or give illustrations of any fibrillation action potentials. These latter, which the English investigator Weddell (1946) has found in electromyograms of the nerves, are of significance both for diagnosis and prognosis. For instance, a decline in the number of these so-called fibrillation action potentials may be a sign of reinnervation of a muscle in which motor units are not to be found. The synchronous motor units may also have prognostic significance. Buchthal and Honcke (1944) have shown that the more extensive the synchronisation is in the initial stage of poliomyelitis, the less favourable the prognosis will be.

In healthy human beings this synchronisation practically never appears.

In an earlier publication (1947) it has been shown that such afferent synchronisation of motor units may be due to a technical error on account of the electric impulses being led from one amplifier to the other. This leakage of current was noted as early as 1934 by the Englishman Matthews. The French authors Lefebvre, Lecoœur and Lerique (1947) have had the same experience, and consequently they use only one channel (amplifier) at a time.

Usually this is of little importance, since we generally lead off from the muscles in which we expect to find activity and from the place at which such activity actually exists. Consequently, the action potentials present in the immediate vicinity, of the electrode will completely dominate the picture. If, however, one electrode stands in an entirely or almost entirely inactive part of the muscle, the diverted action potentials will play a very important rôle. In this way we may very well get synchronous units at the same time. In case of paresis due

to neurological disorders it is quite possible that one electrode will be placed in a relatively inactive part of the muscle. If the other electrode then registers a single motor unit, this unit will give rise to interference and we shall get an apparent synchronisation. As it has been shown by Seyffarth in 1941 and by Lundervold and Seyffarth in 1942 and others that single motor units usually occur in these diseases, it is therefore quite possible that this artificial product may be found especially in these cases. This matter has been more fully dealt with in an earlier publication (Lundervold 1947).

There are three factors which, each in itself, may play a decisive rôle as regards this interference:

- (1) There must exist electrical contact between the electrodes.
- (2) There must exist an electrical connection between the channels (amplifiers).
- (3) The amplifiers must be ordinary grid-earth amplifiers.

The first two factors may generally be controlled. We practically always lead off from the same person, and thus there will be electrical contact between the electrodes. And in order to avoid interference from extraneous electrical sources these sensitive amplifiers have to be earthed, so that electrical contact will exist between the different channels.

Thus it is only the amplifier that can be altered.

Different types of grid-earth amplifiers have been tried with the same results. On the whole, it makes no difference whether the impulses are conveyed direct into the grid in the first tube or through a condenser or transformer. The leakage will be of the same extent in every case, *i.e.* up to 50 per cent, whether the amplifier is worked by battery or by rectifier. It is a matter of indifference whether the needle-electrodes (Adrian and Bronks) are made of copper, silver, or platinum.

Using a push-pull amplifier each input is led to its own particular grid. This mode of recording has been adopted in several experiments, and it is then found that the leakage is reduced to a very small percentage. A push-pull amplifier is therefore quite satisfactory for ordinary clinical electromyography.

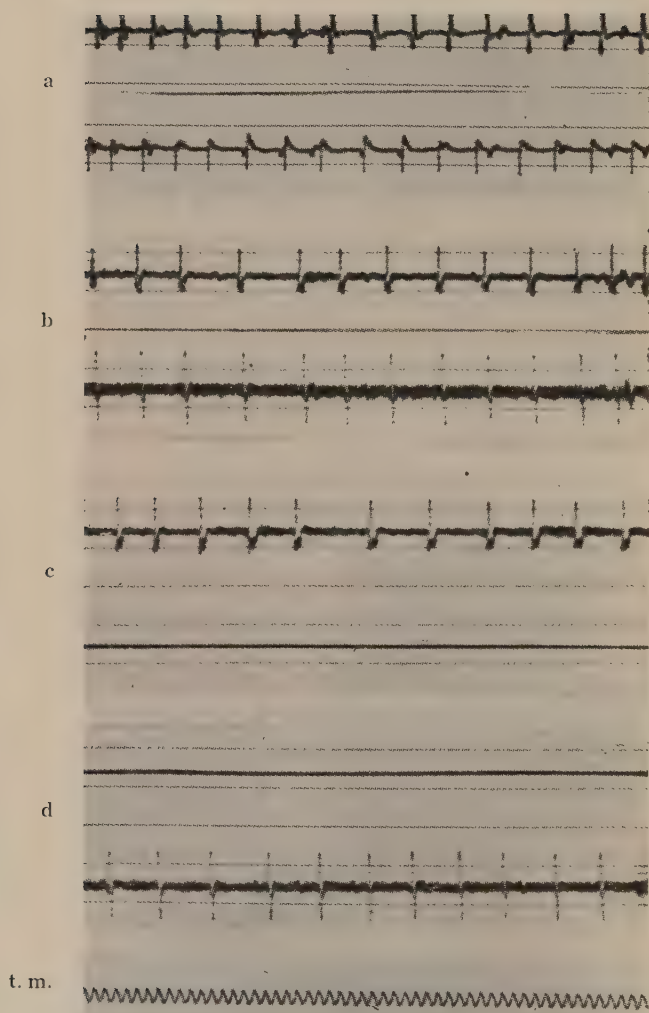


Fig. 1 a.

E.M.G. from a 12-year-old girl with poliomyelitis, registered by two Adrian and Bronk needle-electrodes placed in the m. biceps sin. at a distance of about 3 cm. from each other. Weak contraction. The electromyogram was registered by means of two grid-earth amplifiers.

T.m. = Time-marker $\frac{1}{60}$ sec.

Fig. 1 b.

Same E.M.G. as above, but registered with push-pull input.

Fig. 1 c.

Same E.M.G., but registered only from the proximal electrode.

Fig. 1 d.

Same E.M.G., but registered only from the distal electrode. The patient maintains about the same contraction all the time.

Another, and for research purposes, a better type of amplifier is differential amplifier. There are several types of these amplifiers, described both by physiologists and by electrical engineers (Matthews 1924 and 1938, Matthews and Adrian 1934, Saunders 1942, Parr and Grey Walter 1943, Goldberry 1944 and Buchthal 1945). One of the best and most comprehensive publications on this subject has been written by Denis Johnston in 1947.

A differential amplifier practically precludes the possibility of leakage. Besides having the above-mentioned advantages this amplifier is completely free from extraneous electrical interference, and there is no back-coupling of impulses within the amplifier. The Finnish scientist Bernhard Frankenhauser in a hitherto unpublished work has shown that there may be interference between the channels even with differential amplifiers if they are earthed in more than one place.

As some investigators still use the grid-earth amplifier, it may be of interest to note what errors may arise when they are used. Fig. 1 a shows an electromyogram from a poliomyelitis patient, where the current is led off from the left biceps muscle by two Adrian and Bronk needle-electrodes placed at a distance of about 3 cm. from each other. As is seen, we have here entirely synchronous motor units. The ordinary grid-earth amplifier was here employed. In fig. 1 b

a push-pull amplifier was used, the method of leading off being otherwise the same. The results are alike. Thus we have a real synchronisation, as is also seen in figs. 1 c and 1 d. Here we have led off only from the proximal 1 c or only from the distal 1 d electrode. From both places we register motor units having the same appearance and frequency.

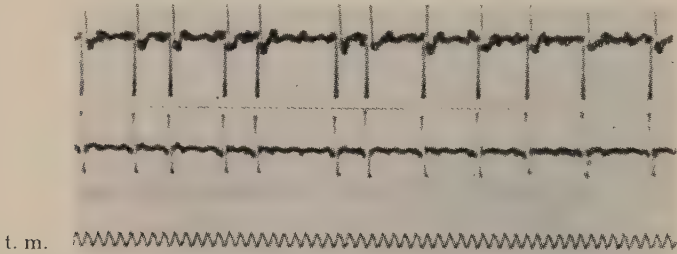


Fig. 2.

Electromyogram from a 16-year-old boy with poliomyelitis. The E.M.G. was registered by two Adrian and Bronk needle-electrodes placed in the m. tibialis anterior dex. at a distance of about 3 cm. from each other, with use of a grid-earth amplifier.

T.m. = $\frac{1}{50}$ sec.

In fig. 2 a we have apparently the same synchronisation of motor units. Here we have also led off from a poliomyelitis patient by means of two Adrian and Bronk needle-electrodes placed at a distance of about 3 cm. from each other. In this case the left tibialis anterior muscle has been examined.

Here a grid-earth amplifier was employed. If we now lead off only from the distal electrode, we get no action potentials at all, although the patient maintains the same contraction, a fact which can be verified by alternately registering with two and with one electrode. Thus the synchronisation in this case is due to the activity existing only in the proximal electrode being transmitted to the other. A similar synchronisation may also be observed in healthy subjects.

This is only one example of the danger of misinterpretation we may incur by using a grid-earth amplifier. Usually this leakage does not play so important a part as in the example

given above, but if it occurs, it will always render difficult the interpretation of the electromyograms.

In all experiments the recording of impulses was made either by two different cathode-ray oscillographs or by one cathode-ray oscillograph with the necessary switching arrangements.

SUMMARY

In the present study it has been shown that, when recording from several different muscles at the same time, there may occur a leakage of electrical activity from one amplifier in an electromyograph to the other. In order that such transmission may take place the following requirements must be fulfilled:

- (1) There must exist electrical contact between the electrodes.
- (2) There must exist an electrical connection between the channels (amplifiers).
- (3) The amplifiers must be ordinary grid-earth amplifiers.

In order to reduce this leakage a push-pull amplifier may be used, or, still better, a differential amplifier instead of the usual grid-earth amplifier.

If sufficient attention is not paid to such leakage, there is a danger of misinterpreting the electromyograms. It has been found that for instance apparent synchronous motor unit activity may be due to leakage of this kind.

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FÜR NEUROPATHOLOGIE DES INSTITUTS BUNGE (ANTWERPEN)
(DIR.: DR. LUDO VAN BOGAERT)

UEBER EINE VESTIBULO-CEREBELLÄRE
ENTWICKLUNGSHemmUNG IM RAHMEN
AUSGEDEHNTER OSTEO-NEURALER
DYSGENESIEN

VON

FRANÇOIS MARTIN
(Genf)

In Ergänzung des von *Koszewski* mitgetheilten Falles von angeborener generalisierter Hyperostose möchten wir an dieser Stelle auf die ausgedehnten Missbildungen und Entwicklungshemmungen des Zentralnervensystems eingehen.

Klinisch zeichnete sich das eutrophische, hypermature, 2 Tage nach der Geburt verstorbene Kind (Geburtsgewicht 4450 gr.), durch eine starke Spastizität und Rigidität aus, die sich besonders deutlich bei Ernährungsversuchen und bei passiven Bewegungen durch anhaltenden Krampf der oberen Extremitäten manifestierten. Eine Hyperreflexie kam wegen der Hypertonie nicht recht zur Geltung. Es bestanden ferner noch Mikrocephalie mit auffallend kleinen Fontanellen, Klumpfüsse, Kamptodaktylie und zwei kindsfaustgrosse inguinale Hernien. Ein Bruder des Patienten leidet an Mikrocephalie und psychische Entwicklungshemmung.

Mikroskopische Beschreibung des Gehirnes: Das Gehirn wiegt in toto 240 gr. und ist in seiner Gesamtheit reduziert. Die Hemisphären sind symmetrisch, die Hirnwindungen an Zahl vermindert, grob und abgeflacht. Die Occipitallappen würden jedoch durch ihre eigene Gestaltung und Ausbuchtung

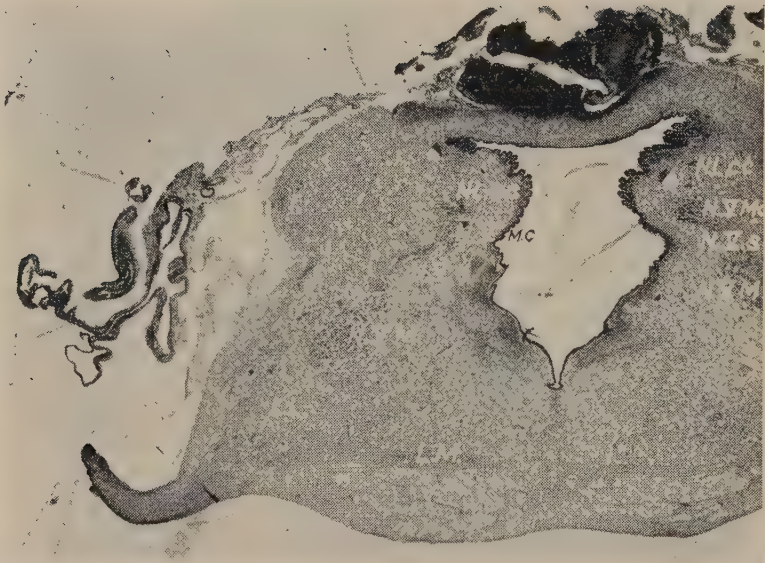


Abb. 1.

Bezeichnung für die Abbildungen (nach Riley: an Atlas ... Williams & Wilkins, 1943).

- B cj — Brachium Conjunctivum
- C rst — Corpus restiforme
- D lm — Decussation lemnisci medialis
- Fb VIII c2v — Fibrae cochleares secundae ventrales
- Fo rg — Formatio reticularis grisea
- Fo rl — Formation reticularis lateralis
- LL — Lemniscus lateralis — LM — Lemniscus medialis
- N Vm — Nucleus mot. nervi trigemini
- N Vs — Nucl. mot. nervi trigemini
- N VI — Nucl. nervi abducentis
- N VII — Nucl. nervi facialis (d, l, v, partes dors., later, ventr.)
- N VIII cv — Nucl. cochlearis ventralis — N VIII vr — Nucl. vestibularis triangularis — N VIII vmc — Nucl. vestib. magno-cellularis (Deiters) — N VIII va — Nucl. vestibularis angularis (Bechterew)
- N X — Nucl. nervi vagi
- N XII — Nucl. nervi hypoglossi
- N d — Nucl. dentatus cerebelli
- N cs — Nucl. centralis super.
- N fc — Nucl. fasciculi cuneati

- N fg — Nucl. fasciculi gracilis
 N glo. — Nucl. globosus cerebelli
 N fs — Nucl. fasciculi solitarii
 N lcc — Nucl. loci caerulei
 N mdfor — Nucl. dissipatus motorius formation reticularis
 N oi — Nucl. olivaris inferior
 N os — Nucl. olivaris super.
 N raphe — Nucl. raphei medialis
 N tg — Nucl. tegmenti cerebelli
 TCS — tractus cortico-spinalis

das Bett für ein relativ normalgrosses Kleinhirn bilden. Pedunculi cerebri sind schmal und leicht dorso-ventral abgeplattet; Brücke und verlängertes Mark symmetrisch, in allen Massen stark verkleinert und deutlich dorso-ventral abgeplattet (Schnittfläche des verlängerten Markes: 7,4 mm frontal). Die Sulci longitudinales sind wenig tief, die Pyramiden aber gut sichtbar. Keine deutliche Vorwölbung an der normalen Stelle der bulbären Oliven. Dem schmalen verlängerten Mark liegt ein auffallend reduziertes, stark abnormes Cerebellum

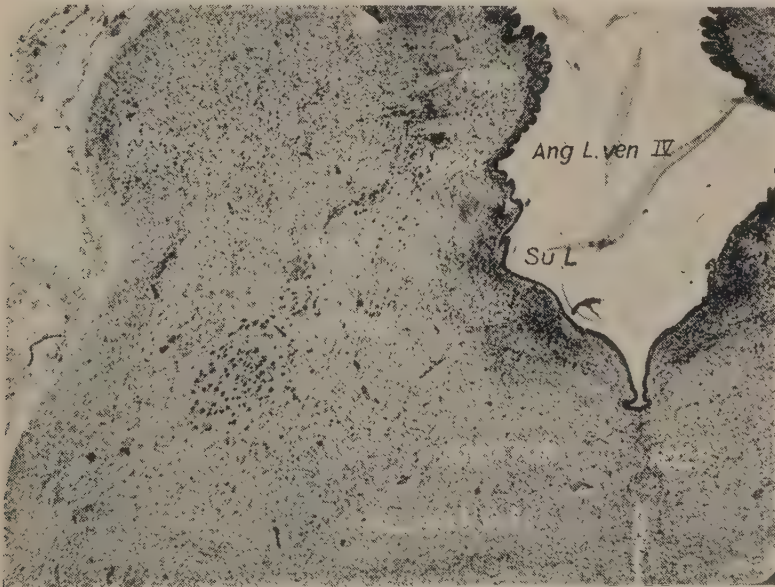


Abb. 2.

auf, das mit der ebenfalls schmalen Brücke durch scheibenförmige wenig entwickelte Brachia Pontis in Verbindung steht. Das Kleinhirn wiegt, samt dem Hirnstamm, 15 gr., ist 28 mm. breit, 15 mm. axiallang und 9 mm. maximaldick. Die cerebellären Hemisphären sind ausserordentlich schwach entwickelt und bilden zwei rudimentäre dorsoventral abgeplattete Flügel zu den verhältnismässig besser ausgebildeten Wurm und Flocken. Die Oberfläche ist auffallend grob, mit an Zahl verminderten transversalen Furchen und ohne deutliche Sublobuli. Die Folia cerebelli sind besser am unteren Wurm erkennbar, sowie andeutungsweise am Culmen. (Abb. 2.)

Sektion des formolfixierten Gehirnes: Grenze zwischen der wenig ausgeprägten weissen Substanz des Centrum ovale und der Markungen und der unregelmässig verschmälerten ca. 2 mm. breiten Rinde deutlich. Basalganglien symmetrisch, im Verhältnis zu den Hemisphären eher gross. Gefässe weit und strotzend blutgefüllt. Ventrikelsystem weit, mit zartem Ependym ausgekleidet. Balken und Fornix schmal. Das Cavum septi pellucidi ist auffallend breit. Der IV. Ventrikel ist ausserordentlich kurz: proximaler und caudaler Pol sind so abgerundet, dass der ganze Ventrikel eine fast halbkugelige Form annimmt. Recessus laterales ventriculi quarti sind breit. Der Ventrikelboden weist nur den sulcus longit. medialis und die sulci laterales auf. Im Dach findet sich ein besser ausgeprägter Wurm. Auf frontalen Schnitten zeigt das Kleinhirn eine undeutliche Abgrenzung der Rinde gegenüber dem auffallend spärlich entwickelten schmalen Mark. Dachkerne und nucl. dentatus sind makroskopisch nicht auffindbar, ebenso, auf weiteren Schnitten, das bulbäre und pontine Grau und die bulbären Oliven.

Mikroskopischer Befund: Das bei der Sektion gewonnene Bild, dass es sich um eine allgemeine Unterentwicklung der Hemisphären handle, wird durch den mikroskopischen Befund bestätigt. Die *Grosshirnrinde* zeigt eine mässig erhaltene Schichtung der Zellanlagen mit spärlichen hypoplasti-

schen Ganglienzellen und einigen Lücken in der Kontinuität, besonders in der Temporalgegend. Die Architektur der tieferen Schichten ist jedoch erkennbar: V und VI zeigen meistens kleine polyedrische Zellen ohne deutliche Dendriten, welche einen kleinen Kern mit grossem Kernkörperchen enthalten. Die pyramidalen Zellen mit globulärem hellem Kern und tigroidem Körper sind auffallend selten, besonders in der V. Schicht, zu finden. Die zwei Körnerschichten sind zellreich und bestehen aus kleinen runden unterentwickelten Zellen. Diese teils hypoplastischen Ganglienzellen sind unter zahlreichen gliaähnlichen Kernen verstreut. Sie weisen die typische säulenartige Organisation auf. Die Windungen sind dabei grob ausgebaut und an Zahl stark vermindert. Die Medialfläche der Hemisphären weist nur zwei Gyri über dem Corpus callosum auf. Die weisse Axe der Windungen ist breit und enthält, unregelmässig verstreut, einige indifferente Ganglienzellen. Die Leptomeninx ist zart und gut ausgebildet, sehr vaskulös, und zeigt weder entzündliche Symptome noch Verwachsungen.

In der *subependymalen Gegend* liegen zahlreiche Keimzentren, welche z. T. perivaskulär angeordnet sind und fingerähnliche radiäre Zellstrassen bilden, z. T., besonders im hypoplastischen Ammonshorn, konfluieren und breite Keimanlagen bilden. (Vergleichend mit einem normal entwickelten Neugeborenen-Grosshirn findet man auch solche Keimzentren, besonders in der Nachbarschaft des Temporalhornes des lateralen Ventrikels, nicht aber in diesem Ausmass). Im *Mark* finden sich noch sehr zahlreiche diffus angeordnete Fettkörnchenzellen, sowie interstitielle Fetttropfen. Das *Ependym* selbst ist regelmässig einreihig und besteht aus grossen kubischen hellen Zellen mit ovalem chromatinreichem Kern. Der Plexus chorioideus ventriculi lateralis besteht aus zahlreichen konfluierenden Keimzentren, welche aus stark zusammengedrückten kleinen polyedrischen chromatinreichen Zellen durchsetzt und oft perivaskulär organisiert sind. Hie und da finden sich in der Umgebung der Keimzentren weiter entwickelte globuläre mit hellem Kern versehene Zellen, sowie unregelmässig zerstreute sehr zahlreiche gliaähnliche Kerne.

In den *Basalganglien* kommt eine gewisse Asymmetrie zum Vorschein: der Kopf des nucl. caudatus ist auf einer Seite schmal und von Bildungsmaterial in Form von Anhäufungen kleiner rundlicher cytoplasmaarmer Zellen mit nur spärlichen differenzierten grossen und kleinen Ganglienzellen durchsetzt. Auf der anderen Seite sind der Nucl. caudatus und die putamino-caudalen Brücken besser ausgeprägt, zeigen aber dasselbe cytologische Bild. Die Grenzen des gliareichen Putamen sind deutlich, durch spärliche kleine inselförmig angeordnete Ganglienzellen gekennzeichnet. Es weist sehr wenige weiter entwickelte Ganglienzellen auf.

Medial vom Putamen wäre die pars pallida nucl. lentiformis zu finden; es lassen sich aber an der Stelle nur sehr schlecht abgrenzbare Zellanhäufungen feststellen, welche aus gehemmtem Bildungs- und Gliamaterial bestehen und keine ausgereifte Ganglienzellen aufweisen. Weiter auswärts liegt die stark gehemmte Insulagegend mit der Capsula externa und dem schmalen aus gliaähnlichen Elementen zusammengesetzten Claustrum. Die Capsula interna selbst ist ausserordentlich schmal und dürftig ausgebaut. Das Balkenknie ist symmetrisch, eher schmal und gliakernreich.

Der Thalamus ist von verschiedenen zahlreichen mittelgrossen polyedrischen hellen Zellen durchsetzt. Ihr Lateralkern ist spärlich bemerkt, enthält aber reife grosse Ganglienzellen. Das Centrum medianum Luysi ist gut ausgebildet. Der thalamische Medialkern enthält sehr spärliche unterentwickelte Ganglienzellen und viele Gliakerne. Das Corpus geniculatum laterale und mediale bds. vorhanden, sowie breite Zellanhäufungen, die dem Pulvinar angehören. Tractus opticus symmetrisch. Nucl. supraopticus bds. durch zahlreiche gut entwickelte Ganglienzellen gebildet. Die paraventrikulären Kerne bestehen aus hypoplastischen Zellanhäufungen. Weitere Kerne der hypothalamischen Gegend zu beschreiben ist gewagt. Corpus Luysi bds. nicht abgrenzbar.

Auf dem vorhandenen Schnitten durch die *Pedunculi cerebri* finden sich weit verstreute Zellen, jedoch ohne Melanin, die keinen typischen Kern bilden, der Lage nach aber dem un-

terentwickelten Locus niger angehören. Andere kleine spärliche Ganglienzellgruppen aus der praectectalen Gegend, mit typischer Gestalt, lassen daran denken, dass es sich um den macrocellulären Anteil des nucl. ruber handle. Ventral liegen nur sehr spärliche hypoplastische Elemente, die den parvicellulären Anteil bilden.



Abb. 3.

Auf denselben Schnitten erkennt man die hintere Kommissur und eine gut entwickelte Epiphyse. Der Aquaeductus Sylvii ist mit einem in voller Tätigkeit befindlichen Ependym ausgekleidet. Die Augenmuskelkerne sind jederseits des Aquaeductus gut entwickelt und die Radix nervi tertii durchquert

das bereits beschriebene Ruberareal. Unterhalb desselben erkennt man den nucl. centralis und diffuse Zellanlagen, die dem undeutlich abgegrenzten Nucl. ruber angehören (Formatio cupuliformis peri-retro-rubrica?)

Die *Brücke* ist ausserordentlich unterentwickelt und besteht lediglich aus einem schmalen Band lockerer transversaler Fasern, die die hypoplastischen Pyramiden umgeben. An

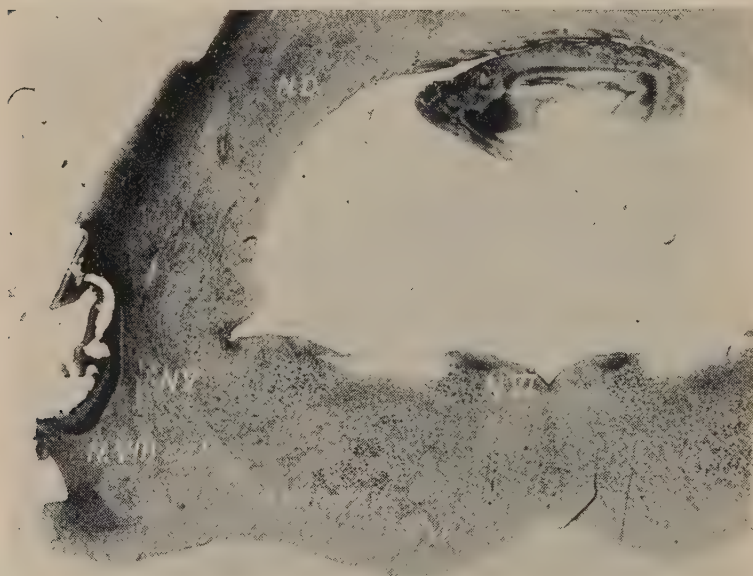


Abb. 4.

ihren lateralen Enden vereinigen sich diese Querfasern und bilden zwei zarte Brachia ad pontem. Verloren inmitten dieser Überkreuzungen von Brückenfasern lagern sich einige verstreute unterentwickelte Ganglienzellgruppen, die dem Brückengrau gehören. Auf demselben Niveau ist die *Kalotte* gut ausgeprägt. Sie weist die Augenmuskelkerne und in der Mittellinie den Nucl. centralis auf. Im Boden des IV. Ventrikels, der die Form eines engen Fünfeckes hat, und auf seinem kleinsten Winkel aufruht, finden sich die Trigemuskern, deren relative Ausdehnung auffallend bedeutend ist (Nucl. V. motor.

dors., principalis, nucl. cephalicus et nucl. sensit.) Dorsalwärts wird der noch hochgelegene Nucl. loci coerulei erkannt, (Abb. 1—3).

Lemniscus medialis und lateralis sind gut gebildet, gliakernreich und bilden die Scheide zwischen der ausgebildeten Calotte und der hypoplastischen Brücke. Auf dieser Höhe finden sich zwei gutentwickelte obere Oliven.

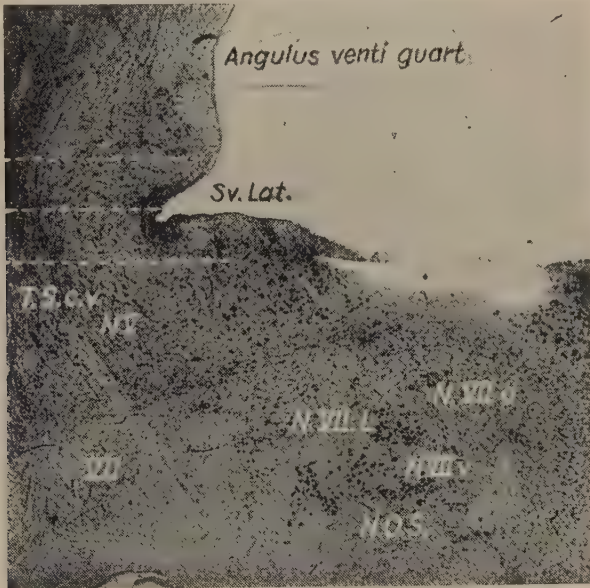


Abb. 5.

Die Brachia conjunctiva sind auffallend wenig ausgebildet. Lemnisci laterales richten sich ausserhalb der brachia conj. gegen die stark abgeflachten und spärlich von Ganglienelementen durchsetzten hinteren Vierhügel. Das Ventrikeldach besteht aus einer relativ dicken schmalen Membran. In der Tat haben die rhomboïden Ventrikellippen ihre normale seitliche Bewegung nicht vollständig durchgemacht.

Im unteren Brückenanteil enthält der Ventrikelboden, neben dem hyperplastischen Trigeminus-system, die motorischen Elemente des Nervus VI und VII, einige verstreute Ganglien-

zellen der *Formatio reticularis lateralis*, und eine eher breite Zellanlage, die einer hyperplastischen *Oliva bulbaris superior* entspricht. Seitlich, zwischen dem *Brachium pontis* und dem *Corpus restiforme* findet sich eine bedeutende Ganglienanlage, *nucl. nervi VIII cochlearis ventralis*. (Abb. 4 und 5.)

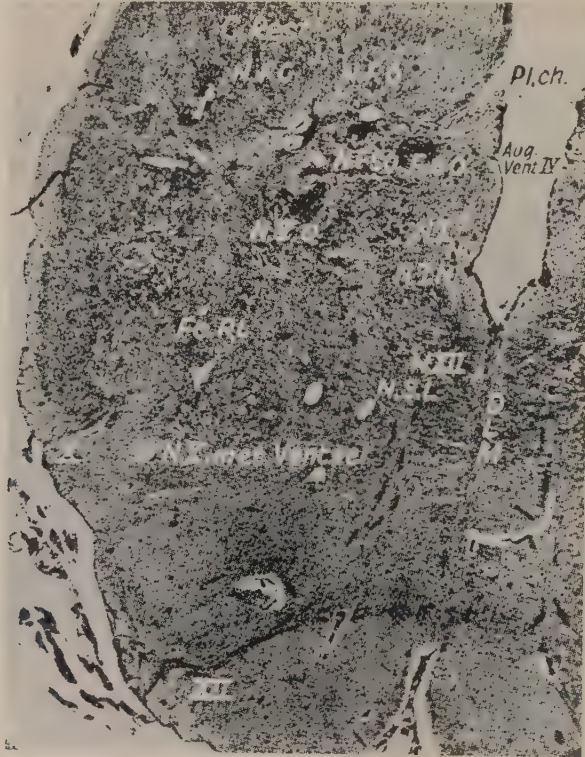


Abb. 6.

Cerebellum: *Pendunculi cerebelli* sind vorhanden, wenn auch auffallend dünn, mit entsprechend gut ausgeprägtem zugehörigem *Corpus restiforme*. Die beiden *nuclei dentati* bestehen aus einer dichten, dreieckigen, gliösen Area, welche nur sehr spärlich hypoplastische dorso-mediale Ganglienzellgruppen ohne deutliche Windungen enthält. Man muss sich fragen,

ob die dominierenden Zellen der Dentatus Area Gliazellen sind oder eher zurückgebliebene Bildungszellen des Kernes, die einem früheren Stadium der Entwicklung entsprechen würden. Die nucl. globosi sind bds. vorhanden, aber in der Entwicklung zurück geblieben. Das Dachmark ist unterentwickelt und der Nucl. tecti wird vermisst; an seiner Stelle findet sich ein lockeres gliöses Areal.

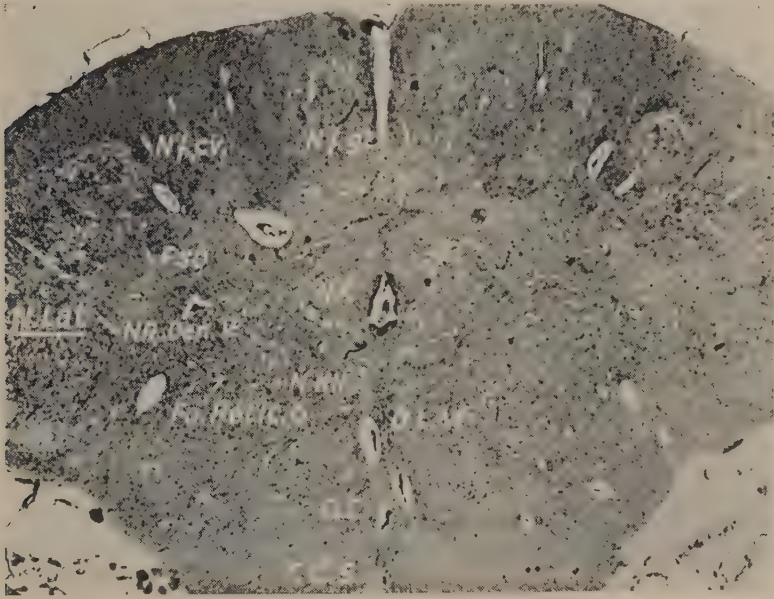


Abb. 7.

Der Wurm besteht aus 5 unregelmässigen Windungen und ist im Verhältnis zu den anderen Anteilen des Kleinhirnes besser ausgeprägt, wenn auch noch sehr klein. Der rostrale Anteil des Wurmes ist bedeutend schlechter ausgebaut, weist weniger Windungen und auffallend spärliche hypoplastische Purkinje'sche Zellen auf. Weiter caudal finden sich eher zahlreiche Purkinje'sche Zellen. Stratum granulare und moleculare sind verschmälert, während die foetale Körnerschicht aussergewöhnlich breit ist. An einer Stelle des Culmen sind weitere Rindenmissbildungen deutlich, mit Zerstörung der

Schichtenstruktur und Bildung eines mosaikähnlichen Bildes. Diese Rindenmissbildungen entbehren jeglicher Purkinje'scher Zellen. Caudal und ventro-lateral prägen sich einige Windungselemente aus, die die Flockenanteile darstellen. (Abb. 8).

Die *cerebellären Hemisphärenreste* lassen den charakteristischen Aufbau nicht erkennen. Es sind nur vereinzelte kleine plumpe Rindengebilde, mit unregelmässiger Schichtung und unreifen Ganglienelementen. Die Purkinje'schen Zellen sind ausserordentlich selten und hypoplastisch; sie erscheinen als grosse helle z. T. fusiforme Gebilde ohne Nissl'schen Körper. Sie liegen zerstreut in der gliareichen Bermann'schen Schicht.

In den Lateralanteilen der rudimentären Hemisphären und des Culmen sind die weichen Hirnhäute mit dem Bildungsmaterial der fötalen Körnerschicht direkt im Kontakt. Die Leptomeninx, die anderorts gut ausgebildet ist, beteiligt sich im Bereichen des Kleinhirnes am Missbildungsprozess. Sie besteht aus einer sehr zell- und gefässreichen Membran mit nur spärlicher Organisation- und Schichtungstendenz. Das Gefässsystem ist, dem Entwicklungsstadium des Kleinhirns entsprechend, unterentwickelt, zeigt aber keine entzündlichen oder degenerativen Veränderungen der Gefässwand.

Medulla oblongata: (Caudaler Anteil.) Das Verlängerte Mark ist auf dieser Höhe leicht dorso-ventralwärts abgeplattet. Die Pyramiden springen vor, während die Eminentia olivaris



Abb. 8.

nur durch eine leichte Vorbuchtung angedeutet ist. *Canalis centralis* ist gut entwickelt und leicht verbreitet. *Pyramidenareal* ist relativ klein und auffallend reich an Gliakernen. An ihrer vorderen Aussenseite sind nur einige *fibrae arcuatae externae* zu erkennen und wenige hypoplastische Zellen, die einen unterentwickelten *nucl. arciformis* vorstellen. Auf der Höhe der *area olivaris* findet man nur wenige Nester unterentwickelter Zellen, die vor allem die dorso-medialen und ventro-medialen Falten ohne Windungscharakter des *nucl. olivaris* darstellen. Im übrigen sind die unteren Oliven nur durch einige Kernanhäufungen vom Gliatypus angedeutet. (Abb. 6).

Der *Lemniscus medialis* und seine Kreuzung sind gut entwickelt und gliakernreich. Voll ausgebildet erkennt man den oralen Pol der Seiten- und Hinterstrangkern, die motorischen Kerne des Vagus und des Hypoglossus, desgleichen den sensiblen Kern des X., den *funiculus solitarius* und seinen Kern sowie die ausgedehnte absteigende Wurzel des Trigemini-Kernes. Die *Formatio reticularis lateralis* ist eher arm an Ganglienzellen. Zu beiden Seiten scheint das *Corpus restiforme* relativ breit und ausgedehnt.

Auf mittlerer Höhe des Verlängerten Markes behalten die Pyramiden ihre oben beschriebene Form. Die *Nucl. arciformes* sind nicht ausgedehnter geworden. Die *Area olivaris*, gekennzeichnet durch eine unregelmässige Verteilung von Gliakernen, ist ärmer an Ganglienzellen als weiter unten geworden. Bald werden die medialen Falten dieses Gebildes gänzlich von Ganglienelementen entblösst. Es sind keine paroliväre Elemente zu finden.

Unter dem Boden des IV. Ventrikels, der sehr eng ist, da sich die Lippen der Rautengrube nicht völlig auseinander gefaltet haben, liegen folgende Kerne: *Nucl. XII*, *Nucl. mot. et sens. X*, *nucl. intermedius*, *nucl. fasc. solitarii*, weiter einige Zellen der absteigenden Wurzel des Trigemini. Das *Corpus restiforme* beansprucht auf dieser Höhe das ganze dorso-laterale Areal. In der Nachbarschaft des letzteren, an der Stelle des *Corpus juxtaestiforme* sind nur sehr spärliche hypoplastische

Zellen gelegen, die dem unteren vestibulären Areal entsprechen. (Abb. 7).

Weiter oralwärts, verbreitet sich der IV. Ventrikel zunehmend, geformt durch die *alae griseae et albae*, die die entsprechende Kerne enthalten. Der *fasc. solit.*, *nucl. V. desc.* und *nucl. ambiguus* sind gut entwickelt. An der Insertionsstelle der *Tela chorioidea*, dargestellt durch eine feine *paucicelluläre* Membran, breitet sich eine verhältnismässig bedeutende Zone aus, charakterisiert durch ein netzförmiges, lockeres und reich vaskularisiertes Gewebe. Dieses ist als die in ihrer Entwicklung gehemmte Knospe des *Plexus chorioideus* deutbar. Sie dehnt sich über das Vestibularareal aus, von dem einzige Elemente gefunden werden können. Desgleichen fehlen auf dieser Höhe die Zellen des *Cochlearis*. Nirgends sind die Gefässe pathologisch verändert.

Vom Rückenmark selbst besitzen wir leider keine Schnitte, sodass wir weder den cerebellären und bulbären, noch den Pyramidenbahnen recht folgen können.

BEURTEILUNG

1. Im Vordergrund der zahlreichen Missbildungen des Zentralnervensystems stehen die symmetrischen Veränderungen des Kleinhirnes und der zugehörigen Anteile und Bahnen: fast vollständige Agenesie der neocerebellären Hemisphären mit starker Unterentwicklung des Wurmes (bes. des rostralen Anteils) und der Flocken; in deren Rinde prägen sich mosaikähnliche Verbildungen aus; enorme Volumreduktion des lateralen Markes; hypoplastische Dachkerne und symmetrische Entwicklungshemmung des *nucl. dentatus*.
2. In Zusammenhang mit diesen schweren Verbildungen steht die symmetrische Hypoplasie der Brückenarme, der Brücke (*fibrae transv. pontis*), des Brückengraus, des Raphengraus, und der *Brachia Conjunctiva*. Das *Corpus restiforme* ist relativ gut entwickelt.

3. Im verlängerten Mark fällt die massive Aplasie der unteren bulbären Oliven, (wenn man auch einige hypoplastische Elemente der medialen Laminae findet), das Fehlen aller afferenten und efferenten olivären Fasern, sowie aller *fibrae arcuatae externae et internae* und des *nucl. arciformis* auf. Die *Nuclei oliv. super.* sind im Gegenteil gut ausgebildet.
4. Im weiteren imponiert eine starke Entwicklungshemmung des gesamten vestibulären Systems. (Siehe Diskussion).
5. Das Trigeminus-Apparat zeigt eine deutliche Hyperplasie aller seiner Gebilde.
6. Im Bereich des Mittelhirnes fällt die starke Unterentwicklung des parvicellulären Anteils des *nucleus Ruber* bei Erhaltung des *magnocellulären* Anteils auf. Der *Locus Niger* und die anderen Kerne der *praectectalen* Gegend sind ebenfalls hypoplastisch.
7. Starke Unterentwicklung des Thalamus, besonders seines medialen Kernes, des Hypothalamus, und des Striatum. Fast totales Verschwinden der *Pars pallida nuclei lenticiformis* und des *Corpus hypothalamicum Luysi*. In diesem Zusammenhang ist wieder der dürftige Ausbau des Brückengraus zu erwähnen.
8. Die Grosshirnhemisphären zeigen Bildungstörungen der ganzen Rinde (Makro- und Oligogyrie, zahlreiche Rindenhemmungen). Mit denselben steht die symmetrische Hypoplasie der Pyramiden in Zusammenhang, wie sie sich an der *Capsula interna*, den *Pedunculi*, der Brücke und dem verlängerten Mark feststellen lässt.
9. Das gesamte Gefäßsystem ist ohne pathologische Veränderung. Die Gefäßwand ist zart, gut ausgebildet und ohne jegliches degeneratives oder entzündliches Zeichen. Einzig weisen die *Plexus chorioidei ventriculi IV.* eine Verzögerung der Entwicklung auf. Sie erscheinen unter der Form von Gefäßknospen, die unter Ependym gelegen sind und keine Vorbuchtung erzeugen.
10. Die weichen Hirnhäute sind im allgemeinen gut ausgebil-

det. Auf der Höhe des Kleinhirns indessen beteiligen sie sich an der Missbildung.

11. Ferner fällt die ausgeprägte Lipophanerose im Hirngewebe auf, welche das Bild einer Virchow'schen Encephalitis bietet. Handelt es sich hier, wie sich aus zahlreichen Diskussionen in der Literatur ergibt, um eine intrauterine, tardive, toxische Noxe, oder eher um einen foetalen Aufbauprozess? Im Falle der ersten Annahme, scheint es wenig wahrscheinlich, dass diese spät in Erscheinung tretende Störung in direktem kausalem Zusammenhang mit den oben erwähnten Hirnverbildungen steht.

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NONDIABETIC GLYCOSURIA IN CHRONIC SCHIZOPHRENIA¹

BY

ELSE MØLLER

INTRODUCTION

Previous investigations into the carbohydrate metabolism in schizophrenics have revealed a number of changes, on the whole only slight and difficult to estimate but still encouraging to further study.

In 1925 *Poul Reiter* going through the previous literature found that glycosuria had been demonstrated several times in psychotics, especially often in manic depressive patients, but also relatively often in schizophrenics. The main result of his own investigations was the demonstration of frequent abnormalities of the carbohydrate metabolism in manic depressives, but besides he found such abnormalities in some cases of schizophrenics, too, though not so often as in manic depressives. He investigated the blood sugar of the psychotics, too, and sometimes he found abnormalities of the tolerance tests.

In the recent literature of the carbohydrate metabolism of schizophrenics the blood sugar concentrations have attracted interest in general, pushing the problem of glycosuria somewhat into the background. A comprehensive review of the more recent literature on this subject is given in the work of *Holmgren & Wohlfahrt* in 1944: "Blutzucker bei Geisteskranken". Further, mention is to be made of two recent papers:

¹ Read at the staff meeting of St. Hans Hospital on November 17, 1947.

one by *Proctor, Dewan & McNeel* (1944) on variations in the glucose tolerance before and after shock therapy in schizophrenia, the other by *Freeman & Zabarenko* (1946) on the outcome of the Exton-Rose glucose tolerance test on 16 patients suffering from acute schizophrenia.

On going through the literature mentioned it is found that disturbances in the carbohydrate metabolism—especially in the form of relatively high tolerance curves under acute exacerbation—are to be found frequently, in particular in recent cases of catatonia and paranoia.

The problem concerning the connection between emotions and the demonstrated metabolic abnormalities in manic depressive patients has been emphasized—in this country particularly by *H. I. Schou* (1937, 1945). A priori, one would perhaps in chronic schizophrenia be less inclined to attach particular significance to the emotional conditions in this respect. On the other hand, we often meet with emotional reactions in paranoics, and it may be that such emotions may be associated somehow with the demonstrated changes in the carbohydrate metabolism.

Poul Reiter (1925) referred to the possibility that renal glycosuria in schizophrenics might be a *constitutional* character with correlation to constitutional factors in the psychosis (cf. the correlation between diabetes, pyknic build, and manic depressive psychosis).

The purpose of the present work has been:

(1) To confirm or invalidate the hypothesis regarding nondiabetic glycosuria being relatively frequent in schizophrenia;

(2) to investigate the character of the nondiabetic glycosurias observed—in particular, whether they are due to a low renal threshold or to a high alimentary blood sugar rise; and

(3) to elucidate the problem whether the glycosuria is secondary to factors such as age or constitution, or whether it is more directly associated with schizophrenia, possibly with certain forms or stages of schizophrenia.

PATIENT MATERIAL AND TECHNIQUE

The case records of 224 patients are analyzed with a view to information about spontaneous and alimentary glycosurias observed accidentally and glycosuria found in glucose tolerance tests.

"Preliminary examination" with ingestion of glucose further has revealed several glycosurias; the glycosurias have been examined with glucose tolerance tests and threshold determination. The results thus obtained are compared with those reported from normal materials, especially the material reported by *Holst*, made up of medical patients and applicants for life insurance.

The material is divided into various groups—according to the clinical picture—that is, form and stage of schizophrenia, age of the patients, duration of illness, etc.—and the results obtained for the various groups are compared mutually and with the normal material.

All the patients are men who for a number of years have been suffering from schizophrenia or schizophreniform psychosis. The concept of schizophrenia is defined only on the basis of the clinical picture and course of the illness, so that the present material contains a number of patients with a history of injury to the head, alcoholism, psychic injuries, psychopathy, inferiority complex, encephalitis, etc. Efforts have been made to obtain a material varied as to age, duration of illness, intensity of illness, and form of schizophrenia, and made up of calm patients and excited ones. In the course of the examinations, however, it has been necessary to exclude some very excited patients. The distribution of the material according to age and year of admission appears from Tables 1 and 2, respectively.

The distribution of the patients according to the form of their illness is shown in Table 3.

The Exton-Rose glucose tolerance test has been applied to a few patients—and to some normal men whose diet did not deviate essentially from the diet of the patients as to carbohydrate content. Especially the last three days before each

TABLE 1
Age distribution of the material.

Age (years)	Number of patients	Number of glycosurics
10-19	1	1
20-29	12	3
30-39	50	15
40-49	77	23
50-59	40	6
60-69	20	8
70-79	2	1

Exton-Rose tolerance test their diet had no essential deviation from the normal average sugar content of the Danish diet.

For three days prior to each test the patients are being watched thoroughly by the personnel: that they are taking their food as usual, not refusing to eat, and that they have no dyspeptic symptoms or signs of acute illness. No test is performed on days when any sweet "fruit soups" or similar dishes have been given to the patient within the previous three days. Owing to war conditions the ordinary diet was relatively rich in proteins, containing less sugar and fat than before the war. In 1945 the patients were given about 700 g. saccharose per week, as against about 900 g. in 1943.

For each patient the interval between the tests was at least 5 days.

On the whole, standard conditions could not be obtained as especially the paranoic patients might get excited, and the catatonic patients get into a state of motor restlessness or exaltation even more frequently. The most excited patients were confined to bed during the test, while the other patients often were allowed to get up because then they could more readily be persuaded to cooperate in the examinations, being in a more agreeable state of mind. As far as possible their attention was drawn towards something else and they were requested to keep quiet. The employment of sedatives was limited to the absolutely required evening or night medicine

given in the evening prior to the test in the form of ally-propynal, medinal, or chloral hydrate—once in a great while, scopolamine-morphine or hypnofen.

TABLE 2
Distribution of material according to year of admission.

Year of admission	Number of patients	Number of glycosurics
before 1916	12	7
1916-20	8	1
1921-25	25	4
1926-30	36	8
1931-35	48	11
1936-40	54	21
after 1940	19	5
1916-30 excited paranoics	13	7
other forms	56	6
1931-40 excited paranoics	17	12
other forms	85	20

TABLE 3
Survey of patient material.

	Number of excited patients	Number of quiet patients	Number of stuporous patients
Hebephrenics	23	52	0
Paranoics	36	33	0
Catatronics	38	5	4
Atypical patients	5	6	0

Possible high or prolonged tolerance curves should not be denied significance on account of the night medicine employed—rather on the contrary. But it cannot be excluded that the night medicine employed may have lowered the kidney threshold and thus given rise to the appearance of glycosuria. In the literature I have been unable to find any work

on the influence of hypnotics on the kidney threshold for glucose.

In some cases doryl was given to promote urination.

All the examinations commenced in the morning at about 8 o'clock, after fasting for about 14 hours.

In 40 cases the urination was not being watched prior to the "preliminary test", because the patient was averse to this or for other reasons. This may have brought about that not all the instances of glycosuria were revealed as a few of these 40 patients really failed to void, so that any sugar-containing urine portion in the bladder was mixed with the fasting non-sugar-containing urine. Naturally this might reduce the urinary sugar percentage below the level demonstrable by means of Almen's test. Indeed, it was possible directly to demonstrate that a couple of my glycosurics, when examined without preceding urination, presented no glycosuria. In the subsequent tolerance test *with* preceding urination these patients again showed glycosuria.

PRELIMINARY EXAMINATION

After voiding in the morning the fasting patients were given 50 g. saccharose. When it was difficult to make the patient take the sugar dissolved in water, the same amount of sugar was given in the form of syrup or, in some cases, as granulated sugar on oat porridge.

Two hours after ingestion of the sugar the patients were told to void and the urine was examined for sugar and albumin. If the patient was unable to void at the right moment—or refused to do so—and objected to injection of doryl, the first portion of urine excreted later on (spontaneously) was used for the examination even if it was voided as late as after 4-5 hours (in one case).

In some cases the glucose tolerance test was performed without preceding preliminary examination and then was taken at the same time as preliminary examination to decide on the presence of glycosuria.

Fehling's test was employed (by the writer) for the examination of the urines in the "preliminary examinations" in 1943, and if the result was dubious, Almen's test was used, too. In 1945 the Almen test was employed (by the same technician who performed the blood sugar analyses). Heller's test was applied to at least one portion of urine from each patient. The tests were carried out exactly as directed in "Klinisk Lab.-Teknik" (1937) by Gram, Iversen & Meulengracht.

In tolerance tests, threshold determinations and Exton-Rose tests, the urine likewise was examined as here described. Furthermore, when glycosuria was reproduced, a fermentation test (Lohnstein) was performed on the urine from 28 of the 57 glycosurics. In some of the other cases, then, the reaction may conceivably have been false.

RESULTS

Altogether 224 case records were studied.

22 patients were either too excited for the examination, or they refused to submit to it.

Glycosuria was found in 51 out of 202 patients. If we also include the 6 glycosurics found on perusal of the case records, and in whom glycosuria could not be reproduced in my experiments, glycosuria was found in 57 out of 202 patients.

The number of glycosurics thus found is the minimum figure, partly on account of the defective control of the urination prior to the preliminary examination in 40 patients, partly because each patient was submitted only to one preliminary examination and glycosuria may appear periodically. (Thus, for instance, on reexamination of 23 patients two years later, only 11 showed glycosuria.)

There is no difference between the frequency of glycosuria found in male schizophrenics and the frequency of glycosuria in mentally normal men examined in the same way.

In his material of applicants for life insurance and medical patients, Holst (1922) found glycosuria in 16 out of 61 men after ingestion of meals rich in sugar; and in his total material of men and women he found glycosuria in 31 out of 159 individuals. In the large material presented by Aage Th. B. Jacobsen (1937) in his "Haandbog for Livsforsikringsmedicin", in which the materials collected by 7 Scandinavian investigators are merged into one, glycosuria was found in 38 out of 174 individuals.

The patients in our material are partly divided in accordance with *Bleuler's* classification, partly grouped into (1) quiet, (2) excited, and (3) stuporous patients. *Bleuler's* hebephrenic and simple are added into one group, which I have designated as "hebephrenic". Besides *Bleuler's* groups there is a group of atypical, schizophreniform psychoses, some of which are quiet, while others are excited. The term "excited" is here used in the sense of agitated, restless, and anxious patients or patients in catatonic muscular restlessness or in affect. So this is a very heterogeneous group.

The catatonic patients in this material are nearly all "excited", very few being stuporous, semistuporous, or quiet. In the quiet catatonic patients, on the whole, the disease has been catatonic in form, but in the period of examination they have been quiet, behaving relatively normally.

Even though this is a very rough classification on broad lines, there were dubious cases in which a clinical judgment was decisive. The state of the patients in the months when the preliminary examinations were performed was used as the basis of their classification into excited and quiet.

With this classification of the material there was found to be preponderance of nondiabetic glycosuria among the *paranoic excited patients* (see Table 4). These patients differ from the other excited ones as well as from the normal material. Besides, they differ from the hebephrenic as well as the *paranoic quiet patients*. No difference was demonstrated between excited *paranoics* and the small group of quiet catatonics, but the possibility cannot be excluded that there might still be some difference that would turn up in larger materials.

The *conclusion* of these findings must be as follows: *The form of the disease and the clinical state of the patients at the time of examination play a role in the frequency of glycosuria observed; and the combination of the paranoic form with the excited state is quite particularly apt to give rise to glycosuria.*

It should be mentioned that the comparisons with the normal materials are not quite reliable because the affected state is not registered in the materials of mentally normal subjects in the literature, so that this group cannot be divided on the same principles as apply to the group of schizophrenics.

FREQUENCY OF GLYCOSURIA IN RELATION TO AGE, DURATION OF ILLNESS, AND OTHER FACTORS

Age.

The frequency of glycosuria in the various age groups appears from Table 1. There are so few patients under 20 and over 60 years that a calculation of the frequency of glycosuria for these age classes would be worthless. The age groups from 20 to 49 years may be dealt with together as they all have the same frequency of glycosuria: about 25-30 per cent.

TABLE 4

Frequency of glycosuria in the more important groups of the material.

	Number of patients	Number of glycosurias
Excited hebephrenics	23	5
Quiet hebephrenics	52	9
Excited paranoics	36	21
Quiet paranoics	33	2
Excited catatonics	38	10
Quiet catatonics	5	2
Stuporous catatonics	4	1
Total	202	57
Normal males in Holst's material	61	16

On grouping the patients according to the form of their disease, the frequency of glycosuria among excited paranoics was found to be 4(9) for the group of 50-59 years, 14(24) for the group of 20-49 years, i.e. there is no demonstrable difference in the frequency of glycosuria between elderly and younger excited paranoics. The frequency of glycosuria among patients with other forms of schizophrenia is found to be 2(31) for the age group of 50-59 years, 21(107) for the group of 20-49 years,

i.e. in these forms of the disease, too, there is no demonstrable difference. If anything, the figures rather suggest a *decrease* in the frequency with increasing age.

Normal materials show an *increase* in the frequency of glycosuria with increasing age.

Duration of Illness.

This factor is difficult to estimate because often the onset of the disease is insidious. Even though the time of admission reckoned from the first manifestation of the disease is variable, the period of hospitalization for the chronic schizophrenics may still be used as an approximate measure for the duration of illness.

The frequency of glycosuria among the patients grouped according to the year of admission is shown in Table 2. The borderline of 1930-31 is drawn for practical reasons, giving a suitable number of patients in the groups.

On grouping the patients according to the year of admission in this way no demonstrable difference between the groups is found.

In this material, *preceding shock therapy* plays no demonstrable role in the frequency of glycosuria.

66 patients had been given shock therapy, and 19 of them had glycosuria. Of the remaining 136 patients 38 were found to have glycosuria. Considering that the two groups—shock-treated and non-shock-treated—differ in their composition because shock-therapy was given especially to patients with excitation phases, the frequency of glycosuria in the shock-treated group is not different from what might be expected.

In the present work no particular consideration is given to the significance of possible *absorptive disturbances*, except that patients with ascertained gastro-intestinal lesions are excluded from the material.

As emphasized e.g. by *Schou* at the Psychiatric Congress in Copenhagen 1946 it is highly probable that affect is often associated with changes in the absorption of sugar from the gastro-intestinal canal; and perhaps the connection between

the excitation and the frequency of glycosuria in paranoids in this material may be found in part in absorptive changes.

Kidney lesions among schizophrenics are of interest because renal glycosuria originally was taken to be associated with renal disease—a view that has been given up by modern authors. Among the 57 glycosurics there were 9 instances of affections of the urinary tracts.

It is very doubtful whether the glycosuria in these cases has had any connection with the lesion of the urinary tract.

Of the 9 patients with lesions of the urinary tracts 3 were hebephrenic, 3 paranoic and 3 catatonic; 5 were excited, 4 quiet.

It cannot be decided whether it plays any role that the patient also has some neurological affection such as certain forms of epilepsy, inferioritas or psychopathia, or if he gives any past history of concussion of the brain or alcoholism. In our material these conditions have been encountered but relatively seldom.

The hypothesis about a connection between glycosuria and leptosomic build may hardly be maintained when (1) glycosuria is found to be equally frequent among normal subjects and among the patients who are chiefly *leptosomic*. On the contrary it is only reasonable to say that it can by no means be excluded that *pyknic* build in the paranoids may have contributed to the particularly high frequency of glycosuria among the excited paranoids.

(2) It may be mentioned that *Mall* (1941) has shown that the blood sugar curves for 10 decidedly leptosomic subjects were somewhat flatter than those obtained for 10 entirely pyknic subjects. If this observation proves to hold good also for larger series of subjects it will go against the idea that glycosuria due to *cyclic hyperglycemia* would occur relatively more frequently in leptosomic individuals.

(3) As will be evident in the results of the kidney threshold examination (see below), it is highly probable that a low threshold is not frequent among schizophrenics. This will largely invalidate the basis for the hypothesis about some connection between *renal glycosuria* and leptosomic build.

GLUCOSE TOLERANCE TESTS AND THRESHOLD DETERMINATIONS

This part of the work has been aimed at excluding possible diabetics from the material and investigating in which cases the glycosuria was due entirely or in part to a low kidney threshold for glucose. Owing to excitement and aversion of the patients to continued examination it has been possible to carry out these studies only to a limited extent.

What has been said about the diet of the patients, the preceding fasting period, and the juncture of the examination in the preliminary experiments applies to the following examinations too. Standard conditions could not be maintained at all, especially not with regard to mental and physical rest during the examination. In the tolerance tests the dose given to all the patients was 77 g. dextrose, corresponding to 70 g. glucose dissolved in 500 cc. water. This procedure was suggested by *Görtz* (1927). Judging from the curves we have adopted the criteria found by *Görtz* for this form of tolerance test, the border values for a normal curve being: Climax 210 mg.%; duration $2\frac{1}{2}$ hours.

In the tolerance tests the blood sugar concentration is determined by the stationary method with tablets as given by *Hagedorn & Norman Jensen*, estimated at intervals of 10-15 min. during the first 90 min., then at intervals for 30 min., and sampling of the blood discontinued after 3 hours. On fasting blood sugar (and in a few other analyses) the determinations were made in duplicate, and when the values deviated more than 5 per cent. they were discarded.

The threshold determinations were carried out by the 2-curve method as described by, among others, *Knud Faber* (1923). The border value for the normal threshold according to this method is 140 mg.%. Still, values of 140-160 mg.% are recorded as relatively low. For each curve conditions were the same as for the tolerance curves, only that the dose of glucose ingested was smaller, and the samples of blood were withdrawn at intervals of 5 min. and discontinued after 90 min.

In the tolerance tests, in most of the cases the patients

could not be made to void more than 2-3 times; and in the threshold determinations they voided at intervals of about half an hour instead of a quarter, making the values obtained for the threshold too high.

In this material no particular significance is to be attached to small deviations of the value. Thus it may be used only for a rough estimation of the type of glycosurics to which the given patients belonged (renal, combined cases, or hyperglycemic type).

Wittkower (1935) thinks that on the whole the emotions have no influence on the form of the blood sugar curves, but on this point he is in conflict with several investigators, *e.g.* Diethelm (1936), Schou (1937), and Cannon (1929).

Even though the blood sugar variations are relatively moderate in the less intense emotions produced experimentally in mentally normal subjects, they may very well become relatively wide in psychotics. In the latter the emotions (state of excitement, anxiety, anger) may undoubtedly attain an intensity that normal subjects will not show in glucose tolerance tests, even though they fear that they may have diabetes.

Muscular activity influences the tolerance curve in a degree that is difficult to calculate.

As to the chronic autistic patients, these conditions are likewise difficult to compare with the corresponding conditions in mentally normal subjects, as, according to Blotner (1945), protracted muscular inactivity lowers the glucose tolerance. Blotner found his patients to show high diabetic-like curves with a late fall and rather frequent glycosuria.

In going through the literature I have noticed nothing about the possible influence of emotions and muscular work on the kidney threshold for glucose. Brems (1928) thinks that he found that adrenalin lowered the kidney threshold, and as the influence of the emotions on the blood sugar curve presumably is due to output of adrenalin from the suprarenals into the blood stream, it is theoretically conceivable that the effect might be something like lowering of the kidney threshold. Still, as will appear from the results obtained in the threshold determination (see below), this does not seem to have been the case in the tests here performed.

Glucose tolerance tests were carried out on 40 patients. In this way the glycosuria was reproduced in 26 patients who on an average showed a relatively large glucose output in the urine, mostly between 1 and 4 per cent.

The results obtained in the 26 patients in whom glycosuria was reproduced are recorded in Table 5.

TABLE 5
Glucose tolerance and kidney threshold in 26 patients with reproduced glycosuria.

The patients No. in material	Tolerance curve		Threshold	Remarks
	Climax mg %	Duration hours		
2	168	<2	165-72	
6	202	2½	151-86	
10	260	1½	188-260	
12	222	2	171-82	
18	181	2	162-81	
19	204	2½	186-204	
21	227	3	135-227	
26	208	>3	154-208	
27	333	<3	254-333	77 years. Diab.?
28	220	<3	165-220	
29	164	<3	150-64	
31	210	2	below 115	
32	184	1½-2	143-84	
35	292	exp. interrupted	200-292	Diabetes?
37	187	2¼	131-87	
41	203	2½	167-203	
42	207	2½	123-82	
45	186	2¼	106-51	*)
46	232	1½	159-71	
47	202	2½	159-202	
51	182	2	153-82	
52	230	<3	below 128	
53	154	1½	below 154	
54	130	1	below 130	
56	173	3	141-73	
57	193	2½	184-93	

In 4 cases determination of the fasting blood sugar concentration failed; in the remaining cases the values obtained

*) frequent vomiting but not before or at exam.

were normal. One patient—a man, aged 77—was presumably diabetic; in another patient the possibility of diabetes could not be excluded, as by mistake the tolerance curve was discontinued after 1½ hours (this curve showed a high rise, and at the interruption it was still at a high level).

The remaining 24 patients would then have to be looked upon as nondiabetic glycosurics. In 10 of them the tolerance curve turned out abnormal—according to the criteria set up by Görtz.

In *Holst's* (1924) material an abnormal blood sugar curve was obtained in 37 out of 83 nondiabetic glycosurics with reproducible glycosuria. So, in this respect, no difference has been demonstrated between the normal material and the schizophrenic.

According to *Aage Th. B. Jacobsen* (1937), in the 37 glycosurics from *Holst's* material, it is reasonable in 13 cases (*i.e.* 16 per cent.) to expect that this condition may later turn into diabetes mellitus, whereas such a development presumably will not take place in the schizophrenics. So the 10 abnormal curves obtained among our 24 schizophrenic glycosurics should not be compared with the 37 out of *Holst's* 83 glycosurics but with 16 per cent. less, *i.e.* with 37 minus 13 = 24 out of 83 glycosurics. The outcome of this comparison, however, remains the same: no difference is demonstrated.

The assertion that a subsequent change into diabetes mellitus probably will not take place in the schizophrenics is based on two points: First, the schizophrenics largely belong to the lean leptosomic type, in which diabetes develops but rarely. Secondly, a review of the literature, as emphasized by *Reiter* and others, shows that diabetes is encountered in schizophrenics but exceedingly rarely if ever.

None of my patients show any clinical signs of diabetes in the form of polyuria, thirst, etc.

It might be possible in larger materials to demonstrate a difference in the frequency of abnormal curves in schizophrenics and mentally normal subjects and in particular, it cannot be excluded that such a difference might be demonstrable if, instead of a mixed material of schizophrenic glycosurics, a material of paranoic excited glycosurics had been investigated by means of glucose tolerance tests and threshold

determination. The present material is too small to allow of any estimation as to whether abnormal blood sugar curves are more frequent in paranoic excited patients than in other schizophrenics and in normal subjects.

Threshold Determinations.

Such determinations were carried out on 43 patients, though, as already mentioned, with too few portions of urine per curve, showing therefore too high values.

As a limit for the threshold the maximum of the tolerance curve has in some cases been employed instead of the special threshold curve. As the tolerance curves on an average keep at a high level, it has not been of any great importance to decide whether their maximum would be, e.g., 210 or 220. In these cases, therefore, I have found it sufficient to determine the blood sugar concentration taken at intervals of 10 min. instead of 5 min. as is otherwise customary in threshold determinations.

In the threshold determinations are included some cases in which the glycosuria was *not* reproduced under the glucose tolerance test, reckoning the maximum of the tolerance curve (which was normal or even higher) as the lower limit of the threshold. The threshold value obtained in this way, of course, applies only to the point of time for the threshold determination, and it does not allow of any conclusion as to the level for the threshold at the point of time when the glycosuria was present. If the threshold be constant for the patients the original glycosuria must have been due to hyperglycemia.

Threshold determination was carried through on the following patients:

- (1) The aforementioned 26 patients on whom the glucose tolerance was carried through, with reproduction of glycosuria.
- (2) One patient on whom the tolerance test was not carried through.

- (3) 15 patients on whom the tolerance test was carried through, without glycosuria being reproduced. The tolerance curve was used as the lower limit for the threshold value.
- (4) One patient in whom the threshold is known to be very low, as he shows fasting glycosuria with normal blood sugar level. The exact threshold has not been determined. Glucose tolerance test not performed.

In 5 of the 43 patients mentioned it could not be decided whether the threshold was below or above the border value for normal threshold, 140 mg.%. In two of them at any rate it was relatively low: below 151 and 154 mg.%, respectively. Reckoning these two patients as having a low threshold, we thus have found *a low threshold in 6 out of 40 patients.*

For the patients in whom glycosuria was reproduced in the tolerance test the results are recorded in Table 5. Among the 24 patients with nondiabetic glycosuria, it was practicable in 19 to decide whether the threshold was above or below 140 mg.%. In 3 it was below 140 mg.%; and in these 3 (out of 19 cases) the results are comparable to the results in *Holst's* normal material. To these three, however, we should add the one patient with fasting glycosuria mentioned above (under 4).

In *Holst's* material, among 83 nondiabetic glycosurics with reproduced glycosuria, a threshold value below 140 mg.% was found in 47, *i.e.* far more frequently than in our material.

Even though this difference may perhaps in part be explained as attributable to the threshold determinations in our material being too high, this can hardly be the whole explanation. At any rate, according to this result, it would be unreasonable to try to explain the frequent glycosuria in schizophrenics by referring to any very frequent low kidney threshold in these patients; it seems more reasonable to look for the explanation in the blood sugar aspects.

The 19 patients on whom complete threshold determination has been carried out as well as glucose tolerance test with reproduction of glycosuria, may be divided into glycosuric types and compared with *Holst's* material. Thus we have

7 schizophrenics with cyclic hyperglycemia	(21)
1 schizophrenic with renal glycosuria	(31)
2 schizophrenics with "transitional glycosuria"	(16)
9 schizophrenics with glycosuria of a less pronounced type	(15)

The figures in parentheses give the corresponding figures for *Holst's* material of 83 patients.

There is no discrepancy between the two materials except with regard to the frequency of renal glycosuria, which is lower in my material than in that of *Holst*.

If the one patient with a very low threshold on whom the tolerance test was not performed be reckoned as belonging to the type with renal glycosuria (or to the combined cases), it will make no difference in the outcome of the comparison.

EXTON-ROSE TOLERANCE

A sugar tolerance test ad modum Exton-Rose was performed on 8 schizophrenics and 10 normal males. The age of the normal subjects was from 22 to 42 years, averaging 32 years, *i.e.* lower than that of the patients.

Both the patients and the experimental subjects were prepared in the same manner as in the preliminary examinations, glucose tolerance tests and threshold determinations. After urination in the morning, the fasting blood sample was taken and, immediately after this, 55 g. "dextropur" (corresponding to 50 g. glucose) in about 250 cc. water was ingested. 30 min. later a sample of blood was withdrawn, and again 55 g. dextropur in 250 g., water was ingested. After 30 min., the third blood sample was taken; then the urine was voided, and it was examined for sugar and albumin. Thus, including the fasting specimens, the test comprises merely 2 urine and 3 blood sugar examinations. So this simple method makes far smaller demands on the patience of the examinees and on the time of the personnel than does an ordinary glucose tolerance test.

In examination of the urine the technique was the same as that employed in the preliminary examinations. The blood sugar determinations were carried out with the technique given by *Hagedorn, Halström & Norman Jensen* (1935) for the stationary method (with reagents in tablet form and with distilled water in all determinations), and with special correction for each portion of thiosulphate employed. All the determina-

tions were made by the same technician who performed the analyses in the tolerance and threshold determinations; they were made in duplicate, and when they differed more than 5 per cent., they were discarded.

TABLE 6
Exton-Rose tolerance tests on schizophrenies

Age (years)	Type of glycosuria	Fasting blood sugar in mg %	30 min. value in mg %	60 min. value in mg %	Sugar in urine
44	Cyclic hyperglycemia	82	117	170	0
42	Less pronounced	65	132	177	0
28	Renal glycosuria	88	154	190	0
50	Renal glycosuria	82	178	156	+
44	Less pronounced	104	160	205	0
26	Cyclic hypergl. (transitional?)	101	157	157	+
35	Cyclic hyperglycemia(?)	102	178	211	+
62	Cyclic hyperglycemia	100	129	170	0

TABLE 7
Exton-Rose tolerance tests on normal males.

Age (years)	Fasting blood sugar in mg %	30 min. value in mg %	60 min. value in mg %	Sugar in urine
34	116	157	159	0
28	106	162	160	0
22	108	147	121	0
42	121	133	164	0
36	108	137	131	0
26	78	143	112	0
27	93	120	185	0
37	95	136	146	0
31	93	124	122	0
40	106	122	157	0

The results obtained appear from Table 6 and 7.

For the sake of comparison it will be appropriate here to cite the criteria given by *Schmidt & Christensen* (1946) for estimation of the findings in Exton-Rose tolerance tests:

Normal curves:

below 170 mg.% in the 3rd blood sample; no sugar in the urine.

Dubious normal:

170-195 mg.% in the 3rd blood sample; no sugar in the urine.

Abnormal curves:

(1) below 195 mg.% in the 3rd blood sample; or (2) + sugar in the urine.

None of my patients showed a perfectly normal Exton-Rose tolerance, but 9 out of 10 experimental subjects did so. So there seems to be a real difference between the two groups, but the material is small, and a further try-out of the method on a larger material is required. If similar results are obtained in larger materials, it will be practicable to employ the Exton-Rose tolerance test as a routine method instead of the ordinary one in scientific studies on the carbohydrate metabolism of schizophrenic glycosurics.

Neither of the two patients with renal glycosuria showed an abnormal 60-minute value, and none of the 4 patients with definite cyclic hyperglycemia showed a normal 60-min. value. On the other hand, however, dubious normal 60-min. values were found in both groups.

All the 8 patients showed glycosuria at the preliminary examination or in the glucose tolerance test in the same summer as the Exton-Rose tolerance tests were performed.

Only in 3 patients glycosuria was reproduced in the Exton-Rose tolerance test, and even though glycosuria is no constant character, this result is still a little striking. Perhaps the difference in the demonstrated presence of glycosuria in the two forms of tolerance tests may be due to the circumstance that in the Exton-Rose test the urine was examined only once after one hour while in the ordinary tolerance test with one dose of glucose it was examined several times and at the preliminary examinations it was examined once after two hours.

That one portion of urine voided one hour after ingestion of glucose need not disclose a nondiabetic glycosuria is illustrated by the following cases in which the glycosuria did not

appear until more than one hour after the intake of glucose: 3 patients, whose urine showed no sugar after 60 min. in an ordinary glucose tolerance test, voided again after 90 min., and now the urine showed: + sugar.

1 patient, in an ordinary glucose tolerance test showed no sugar in the urine after 90 min., but after 125 min. the analysis showed: + sugar.

Presumably analysis of the urine, e.g. after 2 hours in the Exton-Rose tolerance test made on these patients, would have revealed the presence of glycosuria, while one urination after one hour had not shown this phenomenon.

According to Exton and Rose it would seem reasonable in nondiabetic glycosuria to find a 30-min. value that was higher than usual. In our material the 30-min. values are somewhat dispersed, though on an average somewhat higher than the average for the normal subjects.

CONCLUSION

From the findings obtained with the Exton-Rose tolerance test on schizophrenic glycosurics it seems reasonable to draw the following conclusions:

(1) The Exton-Rose tolerance test will in many cases be possible to carry through on psychotic patients while the ordinary test is impracticable.

(2) It seems possible to apply this method for an estimation of the character of the glycosuria in some schizophrenics. In order to establish the serviceability of the method, however, it must be tried out on a fairly large material.

(3) It may be that some minor change in the method is required if it has to be employed as a standard method, as presumably an extra urination, e.g. after 2 hours, will prove of value.

(4) As the emotional reaction to this form of glucose tolerance test is less than to the ordinary tolerance test, it will be of particular value in the examination of psychotic patients. Even though internists may not adopt the Exton-

Rose test as the standard method, it may prove to be of advantage to have it introduced as the normal method in the mental hospital, perhaps in this way: the Exton-Rose test is performed first, and then an ordinary tolerance test is carried out only if the Exton-Rose test fails to give sufficient information.

DISCUSSION OF THE RESULTS

Glycosuria has been shown to be extraordinarily frequent in excited paranoids. No difference has been demonstrated in the frequency of glycosuria in schizophrenics and mentally normal persons. In normal subjects the frequency of glycosuria increases with increasing age, whereas in schizophrenics no difference in this respect has been demonstrated between the younger and the older patients (age group of 50-59 years). In patients with forms of schizophrenia other than the paranoid excited form, the figures obtained are rather suggestive of glycosuria decreasing in frequency with increasing age. No difference has been demonstrated in the frequency of abnormal glucose tolerance curves in schizophrenics and in psychically normal persons; a low kidney threshold appears to be rarer in schizophrenics but it must be admitted that the threshold determinations recorded for this material are too high.

These findings indicate that in the excited paranoids there is a factor that gives rise to glycosuria, and this factor is more closely associated with the blood sugar aspects than with a low threshold.

Conceivably this involves either a primary disturbance in the carbohydrate metabolism, or a secondary disturbance resulting from lacking mental rest during the experiment, possibly lack of other standard conditions, or both. The possible primary disturbance of the carbohydrate metabolism might then be described as a "lability" with wide variation of the blood sugar concentration in the glucose tolerance test, *i.e.*

a high or protracted rise in the blood sugar concentration and resulting glycosuria. A priori we should be most inclined to look for such a disturbance in the intermediary carbohydrate metabolism.

The lack of mental rest during the tests might partly be due to the reaction of the patients to the procedure itself, partly to intercurrent emotions brought about by phenomena in connection with the psychosis.

I am inclined to think that the excited patients in a higher degree than other schizophrenics and normal subjects through their behaviour give expression to emotional reactions connected with the experiments, but this is merely a rough judgment, which is not based on any numerical estimate of the frequency of emotional reactions in this material.

It is open to discussion whether excited paranoics might not be subject to emotional lability,—either merely in the sense that often they have emotional attacks, or possibly in the sense that even on moderate stimulation their emotions are intense.

A vegetative lesion may conceivably form the basis of a possible lability of the carbohydrate metabolism as well as the possible emotional lability; and the two disturbances might be parallel expressions of the vegetative affection.

The frequency of glycosuria among patients with forms of schizophrenia other than paranoic excitement did not increase with increasing age. This observation is also explainable as attributable to a connection between emotions and glycosuria, as among the elderly schizophrenics there are more autistic patients who rarely give expression to emotional reaction. Presumably the autistic patients often have "inner experiences" that may be of emotional character, but in a more established—rigid, not labile—manner.

As an intermediate link between the emotional illusions and the abnormality of the glucose tolerance curve we then may imagine an output of adrenalin from the suprarenals into the blood stream.

A connection between emotional reaction and abnormal glucose tolerance curves has been pointed out in the literature, even though some authors deny the existence of any such relation—or at any rate deny its being of any significance.

In manic depressives after recovery, *Schou* (1937) found abnormal glucose tolerance curves in connection with emotions, accompanied by changes in the sweat secretion and other vegetative aspects.

In schizophrenics these problems have not been investigated to the same extent. In his book about autonomic regulations, *Gellhorn* (1943) emphasizes that schizophrenics often show no blood sugar changes in states of apparently emotional excitement. The findings here presented show that this does not apply to the glucose tolerance of excited paranoics. We have to assume that—in contrast to other schizophrenics—these patients are subject to blood sugar variations under emotions, and that on the whole they perhaps have vegetative disturbances differing from those otherwise occurring in schizophrenics.

SUMMARY

202 chronic schizophrenics are examined for nondiabetic glycosuria after ingestion of sugar. Glycosuria is found in about one fourth of the patients. This is the same frequency as that with which glycosuria is encountered in mentally normal subjects examined in the same way. The incidence of glycosuria varied in the different groups of patients, and it was particularly frequent in excited paranoics. Over one half of the latter showed glycosuria.

In contrast to the findings in normal subjects, the frequency of glycosuria was not greater in the age group of 50-59 years than in younger patients. In patients with forms of schizophrenia other than the paranoic excited form the figures were rather suggestive of a decrease of frequency with increasing age.

No difference was found in the frequency of glycosuria in

patients admitted before and after 1930. Previous shock therapy has not had any influence upon the frequency of glycosuria—apart from the possible indirect influence that may result from the emotional habitus being altered through the treatment, e.g. so that the excitement may subside.

Glucose tolerance tests are performed on 40 patients, and threshold determination on the same number. In 2 patients the possibility of diabetes could not be excluded with certainty (one of them was a man of 77 years).

On 19 patients the glucose tolerance test (with reproduction of the glycosuria) could be carried out as well as the threshold determination, in which the level of the threshold was estimated in relation to the border value for the normal threshold, 140 mg. %.

The results obtained are encumbered with some uncertainty, partly because the standard conditions were met but poorly, partly because it was difficult to get the patients to void sufficiently often in each test.

Among the schizophrenics the incidence of low threshold and renal glycosuria was found to be lower than among the normal subjects, but it must be admitted that the threshold determinations recorded for this material are too high. No difference was found between schizophrenics and normal subjects as to the frequency of abnormal glucose tolerance curves. The incidence of other types of nondiabetic glycosuria—*i.e.* transitional glycosuria and cases of glycosuria of a less pronounced type is not demonstrated to differ from that obtained for normal subjects.

The Exton-Rose glucose tolerance test is performed on a few patients and a few normal subjects. On patients of our category the Exton-Rose test is far easier to carry out than is the ordinary glucose tolerance test. If the results here obtained be confirmed on larger materials, the Exton-Rose test may be of value in scientific studies on the carbohydrate metabolism of schizophrenics.

The cause of the glycosuria is discussed. Presumably emotional excitation may play a role, and this will be unavoidable

because the examination itself provokes it—perhaps especially in excited paranoics, in whom emotional reactions on the whole may be more frequent. Glycosuria may be induced by emotional excitation, or in the excited paranoics there may be a vegetative disturbance that manifests itself partly in an altered carbohydrate metabolism, partly in altered emotional reactions.

The possible vegetative disturbance in the excited paranoics will be in contrast to the vegetative disturbances otherwise assumed to take place in schizophrenics.

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CURARE THERAPY IN SPASTIC CONDITIONS

BY

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Our knowledge of the paralyzing effect of curare comes from the Indians, but its therapeutic employment was long delayed because its composition was unknown. As far back as 1811 and the following years, *Brodie* and other clinicians tried to use curare in the treatment of tetanus, epilepsy, chorea, and spastic conditions. After 1920 several reports have been published on therapeutic results obtained with curare (e.g., *Tsocanakis* 1923 and *Kairiukschitis & Kutorga* 1927). Not until recently, however, has it been practicable to produce standardized curare preparations with the active d-tubocurarine chloride which, depending on the dosage, completely or partially blocks the neuromuscular synapse. Since then, attempts have been made to employ this substance for the combating of extensive spasticity and rigidity. (For details concerning curare and its effect on synapses of the nervous system, see *Prescott* 1947, and *Trier Mørch & Thygesen* 1948).

As early as 1929, *Bremer* demonstrated the electively reducing effect of curare on decerebrate rigidity in animals.

In 1935 and 1936 *West* reported both poor and good results from employment of curare in cases of Parkinson's rigidity and spastic paraparesis. *Burman* (1938 and 1939) is more optimistic as to the therapeutic results in the same lesions,

claiming in particular a dramatic effect in dystonia musculorum deformans. He found a relatively slight rigidity more responsive to the treatment than pronounced rigidity, and he emphasizes the persistent effect for several days after a single injection—something which at a first glance seems unintelligible, as curare is eliminated from the organism within a few hours after its subcutaneous or intramuscular injection.

Bennett (1941) emphasizes the inhibiting effect of curare on spasticity and rigidity and he thinks that with this remedy he is able also to reduce various forms of hyperkinesia (paralysis agitans, athetoid movements, post-encephalitic Parkinsonism, oculogyric crises, Huntington's chorea, and hemiballism). On the other hand, he was unable to confirm the prolonged effect of curare.

The same divergence of the findings is encountered in the two subsequent comprehensive papers:

Under elimination of suggestive factors, *Denhoff & Bradley* 1942 gave curare therapy for 4 months to children in whom spasticity of the lower extremities was the predominant symptom. They found the optimal interval between the injections to be 4 days, and the optimal effect appeared 24 hours after the single injections, apparently because the entirely antispasmodic effect at first is masked by the paralyzing effect of the rather high dosage of curare.

On treating spastic paraplegia after myelitis due to war injuries, *James & Braden* (1946) found the maximal spasm-reducing effect after 30-45 min., and in no instance was there any effect beyond 24 hours. They emphasize especially the favourable effect on spastic pains, but they find 4-5 daily injections required to obtain complete and constant effect.

In order to obtain a protracted effect, *Schlesinger* (1946) gives tubocurarine in oil intramuscularly and finds some reduction of spasms.

So, from the few therapeutic experiments hitherto reported, it appears to be the prevailing view that curare has a spasm-reducing effect, even though opinions are divergent as to the degree and duration of this effect. Furthermore, from the

clinical works available it is not practicable to distinguish sharply between the elective spasm-reducing effect of curare and its paralyzing effect—even though the desired effect at any rate is obtained with doses of curare much smaller than those employed under anesthesia and in psychiatric shock where complete but brief paralysis is wanted.

This apparent divergence may be due to various conditions:

(1) Use of preparations differing in strength and content of active alkaloid.

(2) Differing intensity of treatment with regard to the size and frequency of the dose as well as the total duration of treatment.

(3) Differing selection of the treated cases with regard to the etiology, character, and degree of the spasticity, possibility of spontaneous changes in the underlying lesion, and possible influence of mental factors.

(4) Differing estimation of the therapeutic results, partly with regard to the desired effect—immediate relief from pronounced, perhaps painful, spasticity or more protracted effect in conditions where functional capacity already is restored—partly in relation to what results might be expected in these affections where spasticity or rigidity rarely are found as isolated phenomena, but usually are combined with some degree of paralysis.

Finally, considering the character of the lesions and their possibilities of registration, an estimation of the therapeutic results will to a large extent be based on a subjective judgment of the examiner and examinee.

The purpose of the therapeutic experiments that will be reported here has been to investigate to what extent it might be possible with curare to influence spastic conditions of differing etiology and degree, taking into consideration the possibility of spontaneous remissions and psychic induction.

METHOD

The dosage is selected so that it cannot have any essential paralyzing effect, with intervals between the injections that may be practical and convenient in these preponderantly chronic affections.

Intramuscular injection is employed exclusively. From previous experiences this was found the most favourable method of administration when a protracted curare effect is desired, as subcutaneous injections give an all too capricious absorption of such a potent remedy.

The injection intervals have been from one day to one week.

For estimation of the effect the following criteria have been recorded regularly in direct connection with the injection and with the intervals: Resistance to passive motions of the extremities affected, reflex intensity, extent of the reflexogenic zone of the patellar reflexes, patellar and foot clonus, and functional capacity (especially the gait).

The onset of the paralytic effect is estimated by registration of the cranial nerves whose musculature is known from experience to be paralyzed early by curare: Subjective capacity for accommodation by reading, ptosis, eye movements (diplopia), reactions of the pupils, facial mimics.

Preparations (the choice has been dependent on the availability of the given remedies):

Intocostrin (E. R. Squibbs & Sons, New York) is an aqueous curare extract of limited stability, biologically standardized in "head-drop-cross-over" units, containing 20 units per cc. One unit corresponds to 1 mg. "curare extract", which may give rise to confusion, as 1 mg. of the British and Danish preparations are 3-6 times more active. The maximal single dose here employed has been 2.5 cc. for adults.

Tubarine (Burroughs Wellcome Co., London), stable aqueous solution, containing only the crystalline d-tubocurarine hydrochloride, 10 mg. per cc. Maximal single dose here employed: 1.2 cc. for adults.

Tubocuran. In composition and strength it corresponds to tubarine. As yet it has been applied in one case only.

(In another case quinine methochloride was employed only twice—on account of limited supply. This remedy is no curare alkaloid. It belongs to a group of substances which, probably because of a related stereochemical configuration, have the same inhibitory effect on neuromuscular synapses as has curarine. The substance is given by mouth. Concerning these quaternary ammonium bases and their relation to curare, see Trier Mørch & Thygesen, 1948.)

MATERIAL

Roughly the material may be divided into 5 groups:

GROUP 1

Probably stationary spasticity with some degree of functional capacity (Cases 1-5).

Case 1 (Record No. 1278/47).

Boy, 5 years old, born 22/5/42. Admitted 23/5-19/12/47.

Premature birth in breech presentation. From birth the child was universally rigid, unable to sit at the age of 1 year, but able to stand on crossed legs with support; he could not talk until the age of 4 years. Pronounced spasticity with adductor spasms in lower extremities in spite of resection of obturator nerves and, later, subcutaneous tenotomy of adductors on both sides. In addition, now and then, universal convulsions. The boy has never been cleanly, never able to walk. He was admitted in status epilepticus.

Clinical Exam.: Weight 16 kg.; I.Q. corresponding to that of 3 years. Muscles of back markedly tense. Abdominal reflexes moderate.

Upper extremities: Athetoid movements of left fingers, bilateral increase in tonus, most on left side, where it is partly rigid.

Lower extremities: Very pronounced spasticity, with legs crossed constantly, flexed about 30° in hips and knees. Patellar reflex elicited from entire tibia; lively crossed adductor reflex; no patellar or foot clonus; bilateral Babinski; owing to the spasticity, the possibility of paresis cannot be estimated. He lies on his right side. He can only raise himself on his right elbow; not capable of sitting. Able to stand with support, but only with pes equinus, crossed legs and slightly flexed knees.

Diagnosis: Congenital aplasia of pyramidal tracts (Little's disease).

The character of the lesions excludes the possibility of spontaneous improvement. As the functional capacity is so poor, even slight improvement is likely to be registerable. Relaxing massage is given throughout the period during which curare therapy is tried. Even though the degree of spasticity appears somewhat susceptible mentally, this factor may hardly play any particular role. The treatment falls in 7 periods.

1. *Intocostarin*: 6 inj. of 0.35 cc., increasing to 1.4 cc. about twice a week for 3 weeks. About 10 min. after the individual injections there appears to be some reduction of the spasticity and decrease in resistance to passive motions; in contrast to previous findings, foot clonus can now be elicited, by-and-by throughout the injection interval, too. Degree of patellar reflexes unchanged. After 1.4 cc., for the first time, accentuation of the habitual ptosis. At the end of this period, the heels are brought to the ground in standing posture for the first time.

2. *Intocostarin*: 11 inj. of 1.5 cc., decreasing to 1.0 cc., once a week for 11 weeks. Gradually a sort of walking becomes possible, when the boy hangs on the arms of a nurse. He is just barely able to put one foot in front of the other, but crossing of the legs is still dominant. Effect of the treatment is more striking in the upper extremities which can be moved more freely. The athetoid movements are subsiding, and the boy plays more than before. Spasticity of the back and abdominal musculature subsiding. Still, he cannot sit without being tied to the back of the chair. The spasticity appears to increase somewhat in the course of the weekly injection interval. No distinct difference in the effect of the doses employed except that the ptosis appears after the largest doses. The boy appears somewhat sleepy and flaccid the first hours after the injections.

3. *Intocostarin*: 7 inj. of 1.0 cc. twice a week for 4 weeks. Now, in contrast to before, capable of active movements in hips and ankles. Legs no longer spontaneously crossed. About 10 min. after inj., passive dorsal flexion of feet and abduction of legs to full extent are practicable. Foot clonus increasing in strength. The spasm-reducing effect still appears to be greatest on the day of injection and perhaps on the following day as well.

4. *Tubarine*: 14 inj. of 0.4-0.6 cc. every other day for 4 weeks. No definite ptosis after 0.4 cc., but pronounced after 0.6 cc. Commencing active abduction of the legs though slight. No particular progress in attempts at walking.

5. *No treatment* for 1 week. The masseuse states that the muscles feel harder. Otherwise no definite change.

6. *Tubarine*: 11 inj. of 0.5 cc. every other day for 3 weeks. Able to walk a little in walking-chair, though still with strong tendency to crossing of legs and pes equinus. Spastic resistance to passive motions decreasing; capacity for active motions increasing.

7. *No treatment* for 4 weeks. After 2 weeks distinct aggravation, with return of athetoid movements of left upper extremity. Adduction crossing increasing. Still, the spasticity is distinctly less pronounced than at the commencement of the treatment.

General Impression: The curare effect on the spasticity and athetoid hyperkinesias has been convincing. The patient has been decidedly worse in the period when the treatment was limited to physiurgic measures alone. The favourable effects from the treatment have been obvious to the relatives of the patient, masseuse, nurses, and physicians. It is decided to try whether additional curare therapy together with active exercise and possibly additional orthopedic treatment may improve the functional capacity.

Case 2 (Record No. 1004/47).

Male, 49 years old, pensioned invalid, born 17/6/98. Admitted 2/8-15/11/47.

In 1930, first hospitalization for disseminated sclerosis. At that time spasticity of lower extremities, intention tremor. After this, free from symptoms for 5 years. Since 1935 admitted altogether 10 times to the Neurol. Dep. of the Kommune Hospital under the same diagnosis. He was able to work till 1938. Since 1941 there has been steadily increasing spasticity, spontaneous flexor contractions, painful spasms of lower extremities, especially in the left, with increasingly poor gait; also moderate loss of muscular power in the right upper extremity. Indoors he is able to mowe about by means of two specially constructed supporting trestles.

Cinical Exam., 1947: Abdominal reflexes absent. Slight paralysis of right arm and leg. Right arm atrophic proximally. Right pes equinus in partial contracture; muscle power difficult to estimate. On active flexion in the hip to about 20°, adduction spasms and crossing; on passive flexion in knees and hips, spastic muscular contraction, preventing flexion over 30°, patellar reflexes hyperactive on the left side, elicited on the upper two thirds of the tibia; no patellar clonus, but foot clonus and Babinski on the right side. Able to sit up in bed only with difficulty; moving about, supported in the armpits on two light trestles, which are pushed forwards alternately. The legs can be moved only the distance of one foot, under simultaneous crossing.

The clinical course of the case excludes any spontaneous remissions. Owing to paralysis and contractures no greater functional capacity to be expected, but it seems reasonable to hope for relief from painful spasms and spontaneous flexor contractions.

The treatment falls in 5 periods:

1. *Intocostrin:* 13 inj. of from 1.3 to 2.5 cc. twice a week for 7 weeks. After the 2nd injection the patellar reflexes can no longer be elicited from the tibia. Less power in the left foot clonus, same number of jerks.

Spastic resistance to passive motions unchanged. Not until after 5-6 inj. is there a subjective sensation of more free mobility in the lower extremities; moving about more easily, with less adduction crossing. Spontaneous jerks and pains hardly decreased. When injections are given in the morning the intended effect is greatest in the evening and on the following day. During the inj. day he feels feeble and sleepy, "tired in the eyes" but no objective ptosis.

2. *Quinine methochloride perorally*, altogether 9 g. distributed over 3 days: The patient is examined every 2-3 hours. On the second day, left foot clonus invisible, which has not been possible previously. Resistance to passive motions apparently decreased; the patient thinks that the rigidity has decreased. Possibly suggestive effect has to be taken into consideration, as the patient is given no less than 90 tablets (of 10 cg.) in the course of 3 days. Still, on the third day the patient is able for the first time to abduct the left leg. No untoward effects. The treatment is discontinued because no more of this remedy is available. On the following day the condition of the patient is the same as previously, subjectively as well as objectively.

3. *Tubarine*, 12 inj. of 1.0 cc., increasing to 1.2 cc., every other day for 3 weeks, then 1.2 cc. daily for 1 week. Neither subjectively nor objectively is there any change in the state already attained, especially not in the last week with the daily and increased doses. Under this treatment, discomfort in eyes, up to 2 hours after inj., and increased tiredness in afternoon.

4. *No treatment* for 3 weeks: In first two weeks no subjective or objective changes. After this, increasing rigidity, more difficult manoeuvring and more painful spasms.

5. *Tubarine*, 1.0 cc. daily for 1 week: No noticeable changes. General sensation of tiredness and weakness pronounced. Discharge from hospital.

General Impression: Favourable spasm-reducing effect under the first half of the treatment; then no further improvement. About 2 weeks after discontinuance of the treatment, aggravation of the condition. The favourable effect in the lower extremities is compromised by a sensation of general weakness after the daily inj. Nor does increase of the single dose appear to have any additional spasm-reducing effect. Apparently good effect from quinine methochloride, but the period of treatment is too short for estimation of the result.

Throughout his stay in the hospital, the patient was also given physiurgic treatment. The simultaneous curare therapy is said by the patient to have improved the result as compared to previous physiurgic treatments.

Case 3 (Record No. 580/47).

Male, 35 years old, pensioned invalid, born 20/9/11. Admitted 22/4-7/6/47.

Since 1937, progressive weakness, spasticity, uncertain movements of upper extremities, sphincter disturbances. In 1947 painful spasms in the legs. Since 1942 admitted three times to the Neurol. Dep. of the Kommune Hospital under the

Diagnosis: Disseminated encephalomyelitis (*disseminated sclerosis*).

Clinical Exam., in 1947: Nystagmus. Abdominal areflexia. Upper extremities: Slight right spasticity with hyperreflexia, left ataxia, bilateral dysdiadokokinesia. Lower extremities: Considerably preponderant left spasticity, hyperactive patellar reflexes elicited from the entire tibia, weak crossed adductor reflex, bilateral foot clonus and slight ataxia. Bilateral Babinski. Muscle power good. Gait spastic; able to walk without support.

Long spontaneous remissions are hardly to be expected. Physiurgic treatment under two previous admissions—and also ambulatory—without any particular effect. The patient realizes that a new therapy is being tried; he is perfectly willing to submit to this, but pessimistic as to the outcome. The treatment falls in 6 periods:

1. *Intocostrin*, 6 inj. of 1 cc., increasing to 1.5 cc., twice a week for 3 weeks. Complaining chiefly of constricting nocturnal pains in the calves, subsiding gradually. Without definite relation to the single inj., decreasing spastic resistance to passive movement. Reflexogenic zone of the tibia almost constantly decreasing on the day of the inj. and the following day. Constantly after each inj., decreased power but apparently unchanged frequency of foot clonus. Inconstant transitory accomodation paralysis, once slight unilateral ptosis. He says he walks best on the 2-3 first days after each inj. Discharge from hospital, for further ambulatory treatment.

2. *Intocostrin*, 9 inj. of 1.5 cc., once a week for 9 weeks: for first time in several years he has been riding his bike (30 km.). He walks much better; but when he gets tired he gets tremor of lower extremities. One of the inj. consisted of presumably inactive intocostrin, withdrawn from the usual ampoule, but left for one day at room temperature. On the following day the patient returned and complained of not feeling the usual effect.

Of his own accord, the patient says that he has been able to notice a muscular relaxation in the most spastic musculature, the calves, following the individual inj. This effect was decidedly stronger on the first days after each inj. No changes in the reflexes and clonus. Walking more freely. About 10-30 min. after inj., some glimmering before the eye.

3. *No treatment* for 2 weeks: Return of pain in the calves that had

subsided. Subjective spasticity increasing. Objectively no changes in reflexes.

4. *Intocostrin*, 3 inj. of 1.5 cc. once a week for 3 weeks: again feeling better.

5. *No treatment* for 3 weeks—on account of cold, fever, and confinement to bed: Return of cramp-like pains in calves.

6. *Intocostrin*, 3 inj. of 1.5 cc., once a week for 3 weeks. Gait improved after confinement to bed. Spastic resistance to passive motions almost all gone. Still hyperreflexia and foot clonus. The patient wishes to continue treatment.

General impression: The statements made by the patient are very optimistic. Spontaneous remission seems not probable. The lacking effect from inactive *intocostrin* in the second period of treatment, the relapsing painful spasm on discontinuance of the treatment, and the reflex changes registered in connection with the inj. indicate a definite curare effect.

Case 4. (Record No. 63/48).

Female, 29 years old, single, office clerk, born 24/12/18. Admitted 27/10/47-30/1/48.

Acute attack of severe flaccid paralysis and paresthesia of both lower extremities, accompanied by incontinence of the feces and urine. One month later, commencing spontaneous spastic phenomena in both lower extremities. In the course of 2 months, commencing active mobility. Five times admitted to the Neurol. Dep. of the Kommune Hospital under the

Diagnosis: Sequelae of acute myelitis (chronic relapsing myelitis?).

In 1943 the patient was able to walk a few metres without support. In 1944, aggravation, subsequently improvement. During the last 2 years her condition has been stationary, she has been able to attend her office job. She moves about fairly well by means of two canes, though the walking is inhibited by spasticity and pes equinus contracture. Treated continuously with relaxing massage. In 1947, in the course of a couple of months, again increasing paralysis, involving especially the left knee and foot.

Clinical Exam., 1947: Abdominal reflexes lively. Lower extremities: Muscles slender throughout. Moderate paresis of left knee flexion; dorsal flexion of left foot more paralyzed. Otherwise muscular power fairly good. Muscle spasticity of right lower extremity; more pronounced in left leg, especially of the adductors; almost no active abduction of the legs possible. Bilateral pes equinus contracture. Bilateral patellar hyperreflexia, more marked on the left side, both elicited from the entire tibia; bilateral patellar clonus and foot clonus; bilateral positive Babinski. Slight hyperesthesia of the lower extremities and abdomen. Walking possible only by means of canes, owing to the spasticity.

1. *Tubarine*, 3 inj., of 0.5, 0.45 and 0.4 cc., respectively, at intervals

of one week, ambulatory: no distinct effect on the spastic phenomena. 5-10 min. after each inj., inhibited accommodation; after 0.5 cc., also transitory diplopia, subsiding rapidly. As ambulatory treatment is highly inconvenient to the patient, she is admitted to the hospital.

2. *Tubarine*, 19 inj. of 0.4-0.5 cc. every other day for 6 weeks: During the first half of this period moderate reduction of spasticity after each inj., also reduction in power of the foot clonus. Patellar clonus subsides. In the second half of this period, gradually distinct reduction of spasms, with improvement of the gait. In the right leg there gradually remains only an insignificant adduction spasm. Intensity of reflexes decreasing. Zone of patellar reflex on the tibia decreasing. Slight transitory eye symptoms after each inj., together with moderate degree of universal weakness for 2 hours.

3. *Tubarine*, 8 inj. of 0.5 cc., twice a week for 4 weeks: The clinical condition in the latter half of the preceding period of treatment has kept unchanged subjectively as well as objectively. The state of the patient is best on the day after the inj. The gait is compromised but slightly by the remaining spasm in the left lower extremity. The patient is able to walk about in the room without support, in the corridor with support of one cane. She is discharged from the hospital for ambulatory treatment after a pause.

General Impression: Spontaneous remission may be looked upon as excluded, since the morbid condition has been progressing rapidly during the last two years.

Both the patient and the masseuse state that there has been a spasm-reducing effect from the treatment, more pronounced on the day after the inj., besides a constant improvement of the spasticity, as the patient now walks more freely without support or with one cane, while previously she had to use two canes. Thus there has been a definitely favourable effect, and this improvement may certainly not be attributable to the relaxing massage, which was given for two years without any effect.

Case 5. (Private patient).

Female, aged 18 years, born 11/7/29. Ambulatory treatment.

At the age of 2½ years, attack of "influenza" with high fever and pronounced insomnia during the febrile period. During the following years, the sleep regulation was markedly disturbed. During the last 6 years the gait has been increasingly spastic; the tips of her shoes are worn out within a few days. Now she is unable to run.

Clinical Exam. I.Q. 72. Spontaneous speech of spastic type, test words being chopped to pieces.

Abdominal reflexes fairly lively, equal. Upper extremities: bilateral hyperreflexia with slight left-sided preponderance; bilateral rather severe dysdiadokokinesia. Lower extremities: apart from kneeflexor

paresis, no definite paralysis, slight spasticity on passive motions. Contracture of the feet in equino varus position. Patellar reflexes hyperactive, elicited from the entire tibia; Achilles reflexes inhibited by the contracture; both patellar and foot clonus; Babinski positive on the left side, dubious on the right. Gait markedly spastic (in contrast to the slight spasticity on passive motions) and stamped by the deformity of the feet.

Diagnosis: Sequelae of infantile encephalitis.

Spontaneous remission may be looked upon as excluded. Any particular function of improvement is hardly to be expected on account of the contracture of the feet, where the plantar fascia feels tight and hard. The patient knows that treatment with a new remedy is to be tried.

The treatment, exclusively ambulatory, falls in 3 periods:

1. *Intocostrin*, 11 inj. of 1.5 cc. twice a week for 6 weeks: Each inj. is followed directly by a decrease in the power of the patellar and foot clonus, or the clonus disappears entirely. Further, from the 4th inj., the reflexogenic zone is reduced to two thirds or one third of the tibia. No definite change in the slight spastic resistance to passive motion. About 15 min. after 1st inj., subjective relaxation in the legs, especially the right (in which the inj. was given). Constantly marked tiredness in the legs on the day of inj., but in the evening and, especially, on the following day the walking is said to be more easy. Objectively, no improvement of the gait.

2. *Tubarine*, 2 inj. of 0.6 and 0.7 cc. in the course of one week: On the day of inj. laxness of the legs and universal sensation of tiredness.

3. *Intocostrin*, 3 inj. of 1.5 cc. in two weeks: less "paralyzing" effect; no subjective effect. Objectively, no change in the gait under the entire treatment.

General Impression: Possibly the initial subjective results of the treatment are partly induced. Still, the patient—like other patients—states that the maximum spasm-reducing effect appears on the *day after* the individual inj. As in some other cases, only subjective improvement in the early part of the treatment. No objective function of improvement—perhaps on account of non-susceptible contracture changes. In spite of relatively high dosage periodically, no isolated cranial nerve symptoms. A universal sensation of atony dominates on the day of injection.

GROUP 2

Stationary or progressive spastic affections without particular functional capacity, sometimes associated with spastic pain (Cases 6-9).

Case 6. (Record No. 978/47).

Male, aged 36, pensioned invalid, born 12/10/10. Admitted 14/7-27/10/47.

Since 1930, progressive spastic paraparesis. In 1932 retrobulbar neuritis ascertained. Since 1932, increasing dementia. Since 1943, unable to stand and walk, complaining of paresthesias. In the last years, severe ataxia of upper extremities, together with constant spastic pains in lower extremities. Now completely helpless; he can hardly be placed in a chair. After 1943, twice admitted to the Neurol. Dep. of the Kommune Hospital under the diagnosis: *Disseminated sclerosis*.

Clinical Exam., 1947: Pronounced euphoric dementia. Speech blurred, difficult. Oculogyric instability. Slight paresis of the left side of the mouth. Fibrillation of the tongue. Abdominal reflexes present. Upper extremities: slight paresis of the left hand; bilateral hyperreflexia, incoordination and dysidiadokokinesia. Lower extremities: completely incapable of active movements; legs stiff as planks, owing to spasticity, extended in hips and knees. The possible pareses cannot be estimated on account of the spasticity. Patellar reflexes elicited from the entire tibia; patellar clonus. Achilles reflex absent. No foot clonus. Babinski positive on both sides. The patient is unable to stand or walk.

Thus the lesion has been progressing gradually for 17 years. Increased functional capacity is not reckoned as obtainable. The dementia of the patient makes it difficult to estimate any possible effect on the painful spasticity.

The treatment falls in 5 periods:

1. *Intocostrin*, 4 inj. of 1.5 cc., increasing to 2.0 cc., once a week for 4 weeks: Hardly any reduction of the enormous spastic resistance to passive motions after the individual inj. Intensity of patellar reflexes variable; likewise the extent of the reflexogenic zone. Patellar clonus possibly decreased. No pain in the muscles of the thighs and calves, but still a sensation of tightness, least on the day after inj. No cranial nerve symptoms.

2. *No treatment* for 2 weeks: Perhaps again increasing sensation of tightness. No definite objective changes.

3. *Intocostrin*, 5 inj. of 2.0 cc., increasing to 2.5 cc., once a week for 5 weeks. Statements about possible effects still uncertain. The patient insists upon further treatment.

4. *Tubarine*, 6 inj. of 1.0 cc. increasing to 1.2 cc. twice a week for 3 weeks: Undoubtedly some spasm-reducing effect on the previously almost inflexible lower extremities. No registrable changes in reflexes. Now subjective eye symptoms, "blurring", for a couple of hours after each inj. No ptosis.

5. *Tubarine*, 21 inj. of 1.2 cc. daily for 3 weeks: Spasticity further decreasing. The nurses have less difficulty in placing the patient in a chair. As far as the spasm-reducing effect now allows a better estimation of the patient's condition—and as a paralyzing curare dosage still is far from being reached—there appears to be practically complete paralysis of both lower extremities. Eye symptoms as in the preceding period. The patient is discharged.

General Impression: In the first, not particularly intensive, therapeutic period with intocostirin there were no definite objective changes, but the subjective tightening and painful phenomena subsided somewhat.

Under the last, intensive, tubarine treatment, there is a distinct objective reduction of the spasticity without improvement of the functional capacity—due to the paralysis.

Case 7. (Record No. 1015/47).

Female, aged 24, pensioned invalid, born 16/12/23. Admitted 26/6-25/10/47.

From 1943 numbness and loss of muscular power in the left foot; later diplopia and decreased sensibility of the left 1-3 fingers, tendency to urinary retention and painful spasms. Since 1943 admitted 3 times to the Neurol. Dep. of the Kommune Hospital.

Diagnosis: *Disseminated encephalomyelitis or disseminated sclerosis.*

Since 1943 steady gradual aggravation of symptoms. In 1946 inability to walk. In 1947 confinement to bed. Also increasing paralysis of upper extremities. Now she is unable to eat by herself. Increasing difficulty of speech, gradual loss of sphincter control, euphoria, emotional incontinence.

Chief complaints: Pain in the poplas and painful spontaneous flexor-spasms in both legs, especially the left.

Clinical Exam., 1947: Weight 55 kg. Mentally reduced and euphoric. Rhythmic nystagmus, impairment of vision and papillary atrophy. Loss of abdominal reflexes. Upper extremities: Diffus impairment of muscular power, slight spasticity, intentional tremor, ataxia dysdiakokinesia. Lower extremities: Diffuse atrophy, complete paralysis. Slight spasticity, most on the left side. Hyperreflexia; patellar reflexes from the upper third of the tibia. Patellar and foot clonus. Babinski positive on both sides.

The course of the lesion presumably excludes the possibility of spontaneous changes. On account of the total paralysis of the lower extremities, no functional improvement can be expected. Curare is given in attempts to relieve the spontaneous flexor-spasms and pains in the lower extremities.

The treatment falls in two periods, which may be considered under one.

1. *Intocostrin*: 12 inj. of 1.0 cc., increasing to 1.5 cc., once a week for 12 weeks.

2. *Tubarine*: 5 inj. of 6 cc. once a week for 5 weeks.

On the first day after the 1st inj., reduction in spontaneous spasms. After 2nd inj., legs keeping at rest for 3 days. Since then the effect appears to last throughout the interval between the weekly injections. Still, occasionally spontaneous flexor-spasms, decreasing under the first part of the treatment, stationary in the second period. A couple of times, complaint of "sleepiness" on the day of injection; otherwise no uncomfortable sensations, no ptosis.

General Impression: In spite of the reduced mentality of the patient, there is a definite impression of the pains in the lower extremities being abolished.

Although relaxing massage is given at the same time, the favourable effect from curare is highly probable, as it closely coincides with the institution of this treatment. There is no control pause in the treatment, as the patient strongly insists upon being treated.

Case 8. (Record No. 643/47).

Male, aged 43, pensioned invalid, born 4/8/04. Admitted 1/6-30/7/42.

In 1936 insidious development of paresthesias and numbness and paralysis of the right arm; later, glimmering before the eyes, dizziness, tremor of the right hand, tingling in the finger-tips, difficulty of speech, and impairment of memory. Admitted 3 times to the Neurol. Dep. of the Kommune Hospital.

Diagnosis: Disseminated sclerosis.

The patient was granted invalidity pension in 1939, and the symptoms have been progressing gradually since. From 1945 walking has been practically impossible. He cannot drink by himself. Sphincter control markedly impaired. Increasing dementia. Previously but not during the past six months, painful spasms in the left lower extremity.

Clinical Exam., 1947: Dementia and paranoia, staccato speech. Optic atrophy, anisocoria, coarse nystagmus. Absence of abdominal reflexes. Upper extremities: Moderate diffuse paralysis, more pronounced on left side, distally. Severe intentional tremor and dysdiadokokinesia, with bilateral spasticity. Lower extremities: The muscular power cannot be estimated on account of the very severe bilateral spasticity. Adduction spasms and crossing on attempt at active motions. Patellar reflex elicited by the spasticity; pronounced foot clonus on both sides. Babinski positive on both sides. Walking almost impossible on account of adduction spasms. The gradual progressiveness of the lesion during the last 8 years warrants the exclusion of spontaneous remission. No increase in functional capacity is expected from this treatment, but still the

patient is able to stand on his feet. His dementia will preclude any definite estimation of his own statements.

The treatment falls in two periods:

1. *Intocostrin*: 1.2 + 1.5 cc. after 15 min. 2 days later: 2 cc. 10-15 min. after the injections the reflexogenic zone on the tibia is extended from one third and none to two thirds, and the foot clonus appears to increase in strength, hardly in frequency (signifying a spasm-reducing effect?). After the first inj., perhaps some decrease in facial mimics.

2. *Intocostrin*: 8 inj. of 1.5 cc., once a week for 8 weeks. Decrease in resistance to passive motions, more pronounced on the day of injection and the following day. Reflexes in clonus variable. No noticeable cranial nerve symptoms. Transferred to Nørre Hospital.

General impression: In spite of noticeable reduction of spasms, no functional improvement, which perhaps may be due in part to a contrary attitude and paranoic ideas. The results do not encourage experiments with more intensive treatment.

Case 9. (Record No. 217/38).

Male, aged 25, pensioned invalid, born 5/6/22. Admitted 7/9/36-7/3/38.

On 15/9/36, sudden appearance of flaccid paralysis of both legs, urinary retention and numbness extending up to the nipples. 16/9: Rise in temperature to 38.4°. This condition has been stationary since.

The flaccid paralysis was soon replaced by spastic paralysis, which more recently has been so pronounced as to convey an impression of contracture with slight flexion of the left knee and pes equinus of the left foot. Marked atrophy of the muscles has appeared gradually, and incontinence of the feces and urine has become constant; on account of periodical abdominal spasms which evidently also have affected the pelvis floor, there has also been periodical retention of the urine. Since then the patient has been admitted 5 times to the Neurol. Dep. of the Kommune Hospital on account of painful spasms and spontaneous flexor contractions in both legs.

Diagnosis: Transversal myelitis.

Clinical Exam. (prior to curare treatment, which was carried through at home 1948): Abdominal reflexes absent; complete paralysis of both lower extremities; apparently ankylosis of the left hip, knee and foot joints. Very limited passive motions in the joints of the right upper extremity; tendon reflexes nearly absent. Plantar reflexes weak, normal type. Marked muscular atrophy; analgesia and anesthesia to the manubrium; involuntary passage of the feces and urine.

The course of the lesion excludes the possibility of spontaneous improvement when the therapeutic result is to be estimated.

The treatment falls in 3 periods:

1. *Intocostrin*: 5 cc. twice a week for 3 weeks. During this period

some improvement of the spasms, especially on the day following the injection; after 1 inj., no effect.

2. *Tubarine*: 0.4-0.7 cc. twice a week for 6 weeks. Steady decrease in the spasms.

3. *Tubocuran*: 0.6 cc. twice a week for 2 weeks. Condition unchanged from the preceding period.

After the conclusion of this period, the patient showed a surprising improvement. Now it is possible passively to flex the right hip and knee-joint to right angles and to extend the knee to within 20° of full extension. Passive motions also practicable in the left angle. Tendon reflexes more lively than before; the patellar reflexes can be elicited on the greater part of the anterior aspect of the tibia. The Achilles reflexes cannot be elicited. Plantar reflexes weak. Under the curare treatment, also massage has been given as previously, besides "walking exercises" in a specially constructed apparatus. As a result of this, the muscles of the lower extremities are now more voluminous than in the preceding years.

Further, it is to be mentioned that throughout the period in which the patient was under curare treatment, he was not catheterized, and there was no urinary retention.

General Impression: In this patient no increase in the functional capacity was to be expected, merely mitigation of the spasms. The masseuse states, of her own account, that the spasms have become weaker, so that it is easier for her to massage the patient and give passive motions.

The mother of the patient states that now she notices spontaneous flexor contractions of the legs but seldom, whereas previously there were many contractions daily.

GROUP 3

Cases with spasticity as predominant symptom, and in which the possibility of spontaneous improvement has to be taken into consideration (Cases 10-12).

Case 10. (Record No. 673/47).

Male, aged 44, textile worker, born 9/9/02. Admitted 25/3-2/7/47.

Towards the end of 1946, pains in the right knee for about 2 weeks. Then gradually increasing paralysis and stiffness of the lower extremities, shaking of the legs, and cold parasthesias of the left leg. The condition has been stationary the last couple of months before admission.

Clinical Exam.: Lower abdominal reflexes absent. Marked spasticity of the lower extremities, which are almost incapable of active flexion.

Owing to the spasticity, the muscular power is difficult to judge, but there is hardly any severe paralysis. Patellar and Achilles hyperreflexia, with clonus and patellar reflexes elicited from the entire tibia. Babinski positive on both sides. When supported the patient is able to walk a few steps, the legs mowing like two posts by means of torsions of the trunk. The history of the present illness and the objective findings indicate an acute development of a *myelitic process*, possibly *incipient disseminated sclerosis*, with a great possibility of spontaneous remission. It may be that such a remission has commenced simultaneously with the institution of the curare treatment, about 2 months after admission, when the spasticity was said to be less pronounced.

The treatment falls in 3 periods:

1. *Intocostin*, 5 inj. of 1.0 cc. increasing to 1.5 cc., twice a week for 3 weeks: The spasticity decreases quite considerably, the length of the steps increases, and the last week the patient is able to walk about with one cane. About half an hour after each inj. there is a distinct decrease in the power of the patellar and foot clonus, but the reflexogenic zone is not definitely influenced. In the last week the patellar clonus disappears entirely. The first inj. was followed by transitory headache. 5-10 min. after the second and fifth inj. (1.0 and 1.5 cc.) the accommodation on reading was inhibited, but this subsided in about half an hour. Otherwise no cranial nerve symptoms.

2. *Intocostin*, 4 inj. of 1.5-1.7-1.5 cc., once a week for 4 weeks: Spasticity still decreasing. Reflexogenic zone on tibia reduced to one third. Foot clonus decreasing. The condition remains unchanged throughout the inj. interval. Some inj. followed by slight subjective accommodation paresis. Able to walk a few steps without a cane. Discharged from the hospital.

3. *Intocostin*, 9 inj. of 1.5 cc., once a week for 9 weeks, ambulatory: Further improvement during the first part of this period, condition stationary during the latter part. Now the patient is able to walk about half a km. with one cane. Foot clonus almost all gone. The patient says there is some stiffness of the leg and tiredness of the knees in the last days of the weekly intervals between inj. Possibly slight ptosis 5-15 min. after two of the injections.

General Impression: The improvement may perhaps be due to spontaneous remission. Still, especially towards the end of the treatment, the individual inj. are accompanied by transitory changes which undoubtedly are ascribable to the action of curare.

Case 11. (Record No. 815/47).

Female, aged 46, married, born 21/11/00. Admitted 10/6-5/8/47.

From 1947, increasing general tiredness, dizziness, later decrease in muscular power or right arm, left leg (decreased sensibility), and left

side of the trunk, together with "ache" in the left leg: Unable to work for 3 years. Gait increasingly compromised, especially weakness and stiffness of the left leg. Loss of muscular power in the back; painful spasms in the lower extremities. Imperious micturition. Since 1944, admitted twice to the Neurol. Dep. of the Kommune Hospital.

Diagnosis: Disseminated encephalomyelitis (disseminated sclerosis).

Clinical Exam., 1947: Upper extremities: normal except for slight accentuation of the reflexes of the left side. Lower extremities: moderate diffuse paralysis on the right side, more pronounced on the left. Moderate spasticity on the right side, rather severe spasticity on the left. Patellar reflexes hyperactive, elicited from the entire tibia. Achilles reflex more lively on the right side than on the left. No clonus. Babinski positive on both sides. Gait limping, the right knee giving, the left leg dragging stiffly. Constant complaint of tightening pains in the lower extremities disturbing her sleep. Entire left lower extremity very tender on palpation.

The condition of the patient is not stationary at the commencement of the treatment. Any possible therapeutic result is limited by the pareses. But the spasticity also impedes the functional capacity and causes pain, which perhaps may be mitigated by the treatment.

The treatment falls in 2 periods:

1. *Intocostrin*, 4 inj. of 1.2 cc. increasing to 1.5 cc., once a week for 4 weeks. No objective changes recorded in connection with the individual inj., but after the last inj. the reflexogenic zone is reduced from the entire tibia to one third. The painful tightening subsides already after the first inj. Also on palpation the tightening appears to decrease about 10 min. after the inj. Walking more freely, and finally without a cane for a short distance. The patient states that the effect from the inj. is better on the first day after inj. Objectively the gait does not improve strikingly, being still spastic-paretic. No cranial nerve symptoms. Discharge from the hospital.

2. *Intocostrin*, 3 inj. of 1.5 cc. once a week, ambulatory: Paresis of left lower extremity increased subjectively, probably also objectively. Increasing mental depression on account of her illness, (in spite of continued subjective relief from spastic phenomena). Difficulty in walking prevents the patient from further ambulatory treatment in the outpatient clinic.

General Impression: In spite of lacking functional improvement—because of the progression of the disease and preponderant pareses—there is undoubtedly some effect from curare, subjectively as well as objectively on the entirely spastic phenomena, especially the pains.

Case 12. (Record No. 846/47).

Male, aged 40, laboratory servant, born 14/12/06. Admitted 6/8-8/9/47.

In 1945, transitory vague visual disturbances. During the following

2 years, increasing tiredness of lower extremities; 3-4 months before admission, distinct decrease in muscular power of the left leg and difficult control of this leg; paresthesias of the fingers and of the left foot, together with incoordination of finger movements. For the last 2-3 months, capacity for erection abolished.

Clinical Exam.: Eretic, perhaps euphoric. Abdominal reflexes partially absent. Upper extremities: slight bilateral spasticity, hyperreflexia, incoordination, dysdiadokokinesia, and dysstereognosis. Bilateral moderate spasticity, with patellar reflexes elicited from the entire tibia. Bilateral foot clonus. Bilateral Babinski and Rossolimo. Gait spastic with occasional adduction crossing, otherwise characterized by the left-sided paresis.

Diagnosis: *Disseminated encephalomyelitis (disseminated sclerosis).*

During the period of treatment the lesion is in a labile phase.

The treatment falls in 3 periods:

1. *Intocostrin*, 7 inj. of 1.2-1.5 cc., twice a week for about 4 weeks: Spasticity decreasing during the period of treatment, the reflexogenic zone of the tibia being reduced to one third, but definite changes cannot be recorded in connection with the individual inj. The foot clonus subsides on the right side, the gait improves considerably, and the adduction crossing subsides almost entirely. Better control of the upper extremities. Transitory inhibition of accommodation stated once; another time transitory diplopia about 10 min. after inj. Various complaints of a neurasthenic character, not ascribable to the treatment. Discharge from the hospital.

2. *No treatment* for 3 weeks: Sensitive disturbances developing in the left half of the face. Gradually increasing fumbling, now also decrease in the power of grasping. Again increasing spastic phenomena in the lower extremities. Gait increasingly atactic, with spastic steps, especially the left side. Postural instability.

3. *Tubarine*, 6 inj. of 0.6-0.8 cc., twice a week for 3 weeks: Improvement of gait subjectively, not objectively. No cranial nerve symptoms. Increasing nervousness.

General Impression: No doubt the lesion is in a progressive phase. Under the treatment, no symptoms appear, signifying disseminated processes. The improvement observed in the first period may just as well be ascribable to a transitory spontaneous remission as to the treatment. Variable mental habitus makes it difficult to estimate the condition.

GROUP 4

Case of postencephalitic rigidity with tremor.

Case 13. (Record No. 907/47).

Female, aged 40, born 7/9/06. Admitted 9/6-25/9/45.

Past history negative. Present illness commenced 3 years before with a sensation of tightening in the sole of the right foot and a sensation of contraction of the toes, together with weakness of the right lower extremity. 3 months later, increasing weakness of the right forearm and hand apparently in gradual progression for one year. Since January 1945, admitted twice to the Neurol. Dep. of the Kommune Hospital.

Diagnosis: Chronic epidemic encephalitis (Parkinsonian type); mental depression.

Clinical Exam.: Mentally somewhat variable. Considerable rigidity of all extremities, especially the right arm. Musculature tense and tender. Periodically coarse tremor—without “pill-rolling”—most marked in the right arm, with a tendency to Parkinsonian pyramidal position of the hand. Decreased muscular power of the lower extremities, more marked on the right side, where the deep reflexes are lively, without clonus and without extension of the reflexogenic zone. Parkinsonian gait, walking on the toes.

The course of the illness has been too uneven and the mental state of the patient too labile to ascribe the possible results to the given treatment alone.

The treatment falls in 3 periods:

1. *Intocostrin*, 8 inj. of 1.2-1.5 cc., once a week for 8 weeks. At the same time the patient was given atropine, carbon arc light, and massage. No definite changes can be demonstrated with regard to rigidity and reflexes in connection with the individual injection. After the 8 weeks of treatment, all told, there is distinctly some reduction of the rigidity with a more free gait and now the entire foot is put to the ground. Hardly any diminution of the tremor. No cranial nerve symptoms.

2. *Intocostrin*, 6 inj. of 1.5 cc., twice a week for 3 weeks. Atropine and physiurgic therapy discontinued: subjective aggravation of the rigidity, probably also objective; now the patient walks on her toes again. Tremor increased. Transitory headache and “sleepiness” after the individual injections. No ptosis.

3. *No curare treatment* for 3 weeks. Atropine and physiurgic treatment given again: tremor subsiding gradually, possibly the rigidity, too (at any rate not increased). The pains are said to be about the same in all three periods.

General Impression: Intocostrin has had no effect on the pains, rigidity, and tremor, whereas the tremor has been considerably more

responsive to atropine. The results do not encourage further experiments with more intensive treatment.

GROUP 5

2 cases of myotonia atrophica (Nos. 14 and 15).

Cases 14 and 15.

A male patient, aged 27, and a female, aged 26, suffering from *myotonia atrophica* are tentatively treated with a few doses of *intocostrin* of 1.5 cc., once with 1.2 + 1.2 cc. in 10 min.—without any subjective or objective effect on the myotonic reaction. The double injection was followed by a sensation of dizziness for a couple of hours—possibly signifying accomodation paralysis.

TOTAL IMPRESSION AND DISCUSSION OF THE MATERIAL

1. Effect.

Of all the cases, No. 1 presents a most convincing curare effect and confirms the experiences recorded by *Denhoff & Bradley* that children show greater tolerance for this remedy—at any rate, when given intramuscularly. This is not in agreement with the experiences of the anesthetists with regard to massive intravenous dosage (*Trier Mørch & Thygesen*).

This boy of 5 years, who was treated for altogether 22 weeks, was given doses which per body weight were 5 times as high as those given to the adults treated most intensively, without cranial nerve symptoms becoming particularly more conspicuous. Possibly this may be due to a more rapid excretion of the remedy.

The indisputable therapeutic results with distinct reduction of the spasms and considerable functional improvement are on a line with the experiences of *Denhoff & Bradley* concerning protracted treatment in these age classes. In this case, like *Bennett*, we have been able to reduce the athetoid movements and this is the only case in which the effect apparently keeps increasing throughout the treatment.

Otherwise the main impression from the present cases is that distinct functional improvement appears only after

treatment for some length of time, without increasing particularly in the following period. Thus there appears to be a point of time when no further benefit is derived. Still, as a rule, it will be possible in direct connection with continuous injections of curare to register a spasm-reducing effect; and when, for the sake of control, the curare therapy is discontinued, as a rule an aggravation of the condition appears. In the present material, however, the control periods have been too irregular and too brief to allow of any conclusion concerning this point.

The curare dose which is just sufficient to produce cranial nerve paresis is subject to individual variation, but in individual cases it appears to keep constant from time to time.

With this dose the patients furthermore often complain of general weakness, sleepiness, and uncharacteristic dizziness. The last symptom possibly signifies a slight accommodation paralysis, as this phenomenon disappears almost simultaneously with the difficulty in reading—in 1-2 hours.

With the doses here employed the general weakness and dizziness may sometimes last throughout the day of injection. The ordinary tests of muscular power have not shown any noticeable decrease.

The subjective spasm-reducing effect and functional improvement are almost constantly optimal within the first 24 or 48 hours after the individual injections. This detracts from the possible significance of the mental factor and lends support to the assumption that the paralyzing and spasm-reducing effects of curare are not identical.

With the treatment here employed it has not been possible to demonstrate any changes in the spastic reflex tonus of the extremities. This is in keeping with the experiences reported by *James & Braden*.

Only in cases of almost unconquerable spasticity with abolition of functional capacity (Case 6) is the maximal effect found within the first hours after the individual injections, and the total effect is increased by frequent injections—also in keeping with the experiences of *James & Braden*.

In patients with a lesser degree of spasticity and some functional ability preserved the optimal dose appears to be the one which is just sufficient to produce commencing highly transitory symptoms from the eye muscles and—in concordance with *Denhoff & Bradley*—the optimal injection interval in such cases appears to be 3-4 days.

From the above, the afore-mentioned divergence of opinion in the literature concerning the protracted effect of curare appears to result from differences in the selection of the degrees of spasticity under treatment.

In the present material no patient had such severe painful spasms as to indicate the employment of surgical measures. In 3 out of 4 cases with annoying painful spasms and spontaneous flexor contractions of the extremities a good effect was seen from the curare therapy.

In the only patient treated for postencephalitic rigidity and tremor, no distinct effect from the treatment was noticed. *Burman*, as mentioned, has been successful in his treatment of such rigidity, and so has *Bennett* in various forms of hyperkinesia. Nor have we obtained any favourable effect in myotonia atrophica.

2. *Registration of Effects.*

Even though as a rule it has been possible objectively to register some of the mentioned criteria of reduction of spasms in connection with the individual injections, these objective changes have been so variable that they hardly may be of any value for a routine estimation of the possible curare effects.

Of the objective changes the most pronounced are found in the reflex tonus under the treatment of the more severe forms of spasticity. Here, as a rule, the resistance to passive motions commences to yield after about 10 min., and it becomes practicable to elicit tendon reflexes and clonus which previously had been inhibited by the passive spasticity.

Conversely, in cases with less pronounced spasticity we have seen the reflexogenic zone on the tibia being reduced

after individual injections—though not as any constant and practically serviceable criterion of adequate dosage or effect.

In these less spastic patients, after the individual injections, we have not infrequently seen a decrease in the intensity of the foot clonus without a corresponding reduction in the frequency (this was hardly to be expected either, according to *Sherrington's* theory about the clonus phenomenon being independent of proprioceptive reflexes).

Registration of these conditions requires thorough acquaintance with the spasticity of the individual patient, which to some degree is subject to spontaneous variation—as, for instance, under the influence of psychic factors and tiredness.

Palpation of the firmness of the muscles for estimation of relaxation is hardly practicable for the untrained examiner. As a matter of fact, defective palpable relaxation will hardly be a reliable sign of failing effect, as in these steadily hyperactive muscle presumably the sarcoplasm will increase gradually. Furthermore, besides the active reflex and involuntary tonus, also the passive tonus, dependent upon the position of the extremities, must be taken into consideration.

The electric muscular phenomena are taken to indicate the impulses from the central nervous system reaching the striated muscles (though possibly modified through the nervous transmission and in the neuromuscular synapse).

The aspects of the reflex tonus do not differ fundamentally from those of voluntary muscle contraction. Both the spasticity and the rigidity are considered pathological variants of normal reflex tonus.

Höfer & Putnam (1940) and *Buchthal & Clemmesen* (1945) have been able to stop all electric activity by placing the spastic extremity in suitable positions, and slightly spastic muscles show qualitatively normal reactions on voluntary contraction. *Buchthal & Clemmesen* claim that in these cases the registration of the action potential is no more accurate than the clinical examination. Even in severe cases of rigidity with violent rhythmic tremor, these authors are able to induce complete relaxation by placing the extremities in suitable

position even though these cases show regular signs of disturbances of innervation that can be registered by means of action potentials. Perhaps it may be possible in suitable cases of rigidity to register any curare effect.

3. *Mechanism of the Effects.*

The paralyzing effect of curare was localized already by *Claude Bernard* to the neuromuscular synapse, where the transmission of impulses is blocked by complete "curarization". Later it has been demonstrated that when this substance is given in doses somewhat smaller than required for complete paralysis of striated muscles (including the diaphragm), it can inhibit transmission of impulses in autonomous ganglia and partially block the transmission between pars sympathetic postganglionic fibers and effectors. Curare prevents the normally liberated acetylcholine from acting on the neuromuscular synapse. In still larger doses, curare has a central effect, possibly localized to synapse of the central nervous system (*Trier Mørch & Thygesen*).

Attempts have been made to explain the paralyzing effect of curare by means of electrophysiological and chemical theories concerning the transmission of neuromuscular impulses, and some authors think that curarine and related substances exert their effect by destroying the surface membrane at a susceptible point on the muscle mass in such a way that acetylcholine cannot get to carry out its characteristic rapid depolarization of the membrane. This would give rise to the practically visible phenomenon: the blockade between the motor nerve and the muscle (cf. *Squibb*, 1946).

But this theory does not explain the apparent dissociation between the paralyzing and spasm-reducing effects of curare—a fact that has been confirmed experimentally by *Bremer* on decerebrated animals. He showed that the normal muscular reflex tonus is less sensitive to curare than is decerebrate rigidity.

Possibly the spasm-reducing effect is due to a phenomenon

reminding of *Wedensky's* so-called "inhibition": It may be that curare reduces the capacity of the neuromuscular synapse for transmission of impulses over a certain frequency. In the *partially curarised* muscle nerve preparation, the muscular contraction is normal in response to stimuli under this critical frequency. But increase of the frequency produces blockade, and if the frequency is reduced again, contraction appears once more. Accordingly, the synapse would be able to "filter off" the high frequency stimuli. Applied to clinical therapy, then, the logical consequence of this theory would be that we should aim at curarizing the synapse to a point where it blocks all impulses with a frequency higher than that for normal voluntary contractions.

As yet this theory is at its experimental stage, and it offers no explanation of the prolonged effect demonstrable in earlier materials as well as in the present one.

Because of its rapid excretion, a direct curare effect will presumably be out of the question.

Provided this clinical experience holds true, its explanation will possibly have to be looked for elsewhere in the spinal reflex arc outside the neuromuscular synapse. The initial partial curare blockade in the synapse reduces the hyperactivity in the reflex arc; and once it is broken, it will perhaps take some time for restoration of its full activity—no matter whether the cause of this is to be looked for in the ascending discharge of the kinesthetic receptors, in summation of the spinal reflex center, or elsewhere in the reflex arc.

Anesthesiology and experimental experiences with intravenous injections furnish no evidence of cumulative or prolonged effect of the substance—apart from the fact that curarization may be repeated within 1-5 hours with a somewhat smaller dose of the remedy.

The lack of effect in the cases of myotonia here treated tentatively is probably due to the circumstance that the underlying affection is located in the muscle itself or in the muscular part of the motor end plate.

Brown & Harvey have curarized goats presenting signs of

congenital myotonia (corresponding to congenital myotonia in man) without obtaining any effect.

CONCLUSION

From the above it seems reasonable to keep on with tentative curare therapy in patients with spastic affections. A particularly encouraging therapeutic result was obtained in the case of a 5-year-old boy with Little's disease. Functional improvement has been observed also in patients suffering from disseminated sclerosis with spasticity as the predominant symptom. Furthermore, subjective relief from spastic pains has been obtained in some cases. On the other hand, no favourable effect was noticed in a patient with postencephalitic rigidity. No favourable effect was observed in myotonia atrophicans—nor was any such effect to be expected, considering the cause of the lesion.

Curare therapy cannot replace the physiurgic and orthopedic treatment, but merely serve as a supplement to such treatment as it is easier to treat the secondary myoses, and more convenient to give passive or active motions when the muscles are relaxed. Further, it is practicable with curare therapy to increase the muscle power by exercise in slightly paretic muscles, where hitherto spasticity precluded the employment of this measure.

Finally, curare therapy appears to be a valuable measure by abolishing or mitigating the painful spasms which to the patient often constitute the most annoying symptom, and in this way the treatment may also be of great value to the totally disabled patients with stationary spasticity.

In our scanty material we have found individual differences in the tolerance for curare, but the tolerance appears always to be the same in the same patient.

From the results obtained the optimal dose appears to be the one that is just sufficient to give eye symptoms (accommodation paresis and slight ptosis) without any more severe or universal paralysis, given at intervals of 3-4 days.

The initial dose for adults is about 1.5 cc. (30 units) intoastrin or 0.5 cc. (5 mg. tubocurarine hydrochloride) turabine or tubocuran intramuscularly.

In ambulatory treatment we have given the injections once a week; under this regime the spasms have been increasing the last days of the interval, prior to the next injection.

It would mean a great relief to the patients if the curarizing action of quinine methylchloride in further experiments would prove to hold true, as this drug can be taken by mouth. Hitherto, however, the amount of this substance at our disposal has been very limited, and we therefore wish to emphasize that further experiments with this remedy ought to be carried out when larger amounts of it become available.

Even though curare therapy is merely symptomatic, a supplement to the physiurgic-orthopedic treatment, and even though we have found it ineffective in postencephalitic rigidity, the preliminary results from this therapy in spastic conditions have been so encouraging as to call for a further try-out of this therapy.

SUMMARY

A brief survey is given of the literature on coniin and curare, and mention is made of purified curare preparations produced in recent years.

A fairly detailed account is given of the effect of curare on 14 patients with spastic affections of various etiology (Little's disease, disseminated sclerosis, postencephalitic rigidity, and myotonia atrophica) and restoration of different degrees of functional ability.

Reduction of spasms and mitigation of spastic pains are obtained by intramuscular injection of about 1.5 cc. intoastrin and 0.5-0.8 cc. tubarine or tubocuran. The spasm-reducing effect lasts for a few days—in contrast to the universal paralyzing effect of curare, which with this dosage is only slight and disappears within one hour.

Mention is made of the spasm-reducing effect of quinine

methochloride, which is active also when given by mouth. Unfortunately, only a very slight amount of this substance has been at our disposal.

The therapeutic results reported in the literature and those obtained in the present scanty material encourage a continuation of the therapeutic experiments with this remedy in cases of rigidity and spasticity of various etiology.

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**Comments on the Diagnosis of
Chronic Painful Conditions with a Report of
Two Cases of Obscure Pain**

*(Chronic Deferentitis Giving Rise to Ureteric Pain and Chronic
Maxillary Abscess without X-ray Signs of Osteitis)*

By

JACK ADAMS-RAY

After having—in one's own opinion—thoroughly examined a case of chronic severe pain without discovering the source of the pain, one is apt to think of psychopathy or perhaps malinger.

Before deciding upon such a diagnosis it is, however, wise to ask oneself once more whether all diagnostic possibilities have been taken into account.

Not infrequently the *history* has not been taken carefully enough. Recently I have seen two such cases in which a diagnosis had not been made because of an incomplete history. In the first case the patient had consulted another clinic because of "heat" of the foot of one year's standing, and had been advised *inter alia* to bathe the feet in cold water. Further questioning disclosed that the "heat" was intermittent burning pain. The cause was endangiitis. In the other case the patient had had pain in the hips for 5 years, and X-ray showed mild *malum coxae*. He had consulted several physicians, and among other things arthrodesis had been suggested. When his symptoms were thoroughly investigated, they proved to be intermittent claudica-

tion with the pain localized in the hip region, and the diagnosis of endangiitis was confirmed by arteriography.

Although the history has been carefully taken, the *analysis* of the patient's pain may be at fault. By way of an example it may be stated that such faulty analysis is probably one of the reasons why patients with typical chronic, recurring volvulus of the sigmoid flexure—a disease which is by no means rare—may have to bear their severe pain untreated for years—even up to 40-50! If their pains are analysed, it is clear in nearly every case that it must be a question of recurring intestinal obstruction. If X-ray fails to afford a definite support to the diagnosis—and that is not infrequently so—operation may be done on the basis of the history, and the diagnosis verified by the changes in the mesocolon.

Even the *clinical examination* including the *X-ray examination* may have been incomplete.

A more accurate inspection and palpation may at times lead to the diagnosis.

For instance, a patient who for a long time had been suffering from pain in the foot "as soon as he put his shoe on", was found upon careful palpation to be affected with a subcutaneous tumour of the sole of the foot with intensive radiating pain, typical of glomus tumour, upon pressure on the growth.

As regards X-ray examination, professor Söderlund has adopted the principle of a *complete* X-ray examination in cases of obscure, chronic abdominal pain: heart, lungs, kidneys, gall-bladder, colon, stomach, and perhaps examination of the passage of barium through the digestive tract. In a large number of cases this principle has proved of great benefit to us as well as to the patients.

The old truth that pain typical of a disease may be caused by morbid changes in another organ is also often overlooked. Often patients with typical symptoms of gastric ulcer, but negative X-ray findings remain untreated until X-ray of the gall-bladder at last reveals calculi. Or *vice versa*.

Gastric ulcer penetrating to the pancreas and giving rise to backache *only* also belongs to this category.

The value of renewed X-ray examination some time after a negative examination cannot be emphasized too much. Negative X-ray findings in a male older than 50 with "rheumatic" backache and negative findings on rectal palpation do not justify one in minimizing the complaints. Renewed examination after the lapse of some time may lead to a diagnosis of cancer of the prostate with metastases.

Access to a first-rate radiologist with a superior technique also involves a certain danger.

If daily verification of the X-ray findings on the operating table has taught one to rely on the X-ray diagnosis, the written report: negative X-ray findings may lead one astray. Even the most skilful radiologist may be mistaken, and X-ray cannot demonstrate everything! This is self-evident, but it is not always borne in mind. A very large gastric ulcer or one which is at once extensive and shallow may escape even the best radiologist.

Taking another example, the X-ray film of a gall-gladder filling and emptying in a normal way with no demonstrable stones does not always exclude the possibility of cholelithiasis.

A case with typical gall-stone attacks and a gall-bladder found to be normal on the X-ray film and on palpation in the course of exploratory laparotomy was treated as suffering from biliary dyskinesia. Upon renewed laparotomy the gall-bladder was found to contain a few, small, rather soft calculi. It was removed and the patient has since then been symptomless.

When a case remains unelucidated after regard has been paid to all the factors mentioned, we have still a means at our disposal, one which we all know, but regrettably do not always think of, *surgical exploration*.

I shall now proceed to show its value in two cases of obscure, protracted pain. As far as I have been able to find out from a study of the literature available during the time at my disposal,

these cases are unique, and therefore I feel justified in publishing them.

Case 1. A male, aged 52, who 20 years ago had an uncomplicated gonorrhoea. Thirteen years later acute retention of urine. He was treated with catheterization at another hospital. Since then he had not had any difficulty of urination worth mentioning.

From 1942 the patient had been suffering from attacks of severe, spasmodic pain in the lower abdomen, mainly on the right side, radiating partly into the scrotum and the inside of the right thigh, partly into the back on a level with the iliac crest. As a rule the pains lasted for 20 minutes up to a couple of hours, being continuous with occasional intensive exacerbations. They were so severe that the patient could not stand erect. They were brought on by hard work, coitus, or defæcation. There were symptomless intervals, sometimes of 3-4 days.

I saw the patient at the beginning of 1946. Intravenous pyelography, X-ray examination of the gall-bladder, colon, stomach, and intestinal passage showed nothing abnormal. No pathological components in the sediment. Perhaps some thickening of the epididymis on both sides. Otherwise nothing abnormal. The mild bilateral epididymal changes were not considered to account for the patient's complaints.

Later in the same year the patient consulted another surgeon who performed bilateral epididymectomy. Microscopical diagnosis: Chronic unspecific epididymitis. At first there was some improvement, but the pains returned in the same way as before. Renewed pyelography negative. He was using large doses of analgetics.

At the beginning of 1948 the patient again came to me. At that time his pain was so severe that he was hardly able to look after his work and was contemplating suicide. Renewed examination revealed, in addition to a small right-sided indirect hernia, tenderness in the right lower quadrant of the abdomen, increasing in intensity down towards the right inguinal region where there was marked tenderness.

Operation on Jan. 21, 1948: *Resection of the vas deferens, herniorrhaphy, appendectomy.*

Incision in the right inguinal region. Indirect hernia, as large as a pigeon's egg. Its medial, lower edge was broadly and firmly adherent to the vas deferens which was thickened by fibrous scars up to the size of the kernel of a date. The vas had to be detached from the peritoneum with sharp dissection. Herniorrhaphy. Old adhesions towards the vermiform process which was extirpated. Microscopical diagnosis: Chronic inflammatory process of the vas deferens.—The appendix revealed a somewhat sclerosed submucosa, but there were no signs of appendicitis or periappendicitis.

The patient has had no attacks of pain after the operation.

Discussion: The severe pain in the 1st lumbar segment suggested most of all colicky pain due to ureteral affection. The

negative results of the examinations, however, spoke against such a diagnosis. I was convinced that it was not a case of psychopathy or malingering, as I had repeatedly seen the patient have his attacks while he was working outside my house. He doubled up with pain, his face turning absolutely white.

In 1946 I regrettably never thought of exploration, perhaps mainly because none of the findings indicated the presence of a localized process which might give rise to the pain.

The adhesions to the appendix, which was found to be affected with negligible patho-anatomical changes, could probably, and almost positively, not have been the cause of the pain.

Acute deferentitis may cause pain of this type, and *Geierstam* has published a case of subchronic hæmaturia and lumboinguinal pain which proved to be due to chronic vesiculitis.

The protracted duration of the painful condition in my case and the way in which the attacks were brought on did not indicate that the chronic inflammatory process as such was the causative factor. In this case one was struck by the broad, firm adhesion between the vas deferens and the parietal peritoneum with possibilities of a mechanical tension on the sensitive peritoneum. It is a matter of experience that tension on the mesocolon with consequent stretching of the peritoneum may cause severe pain. In hernia too, pain of this genesis is met with, and particularly in the early stages there may be rather severe pain. In the case under discussion the pain was often brought on by factors which might induce tension of the vas deferens and of the peritoneum as well because of the adhesion.

Lastly, the result of the operation supports the theory that the painful condition was caused by the chronic deferentitis with adhesion to the parietal peritoneum.

Summary of the Case: A male, aged 52, with a history of severe right-sided, disabling pain resembling ureteral colic, at last causing extreme psychic depression. There was also a history of urinary tract disorder. Complete X-ray examination was negative. No pathological components in the urinary sedi-

ment. No definite positive findings on the whole. Bilateral epididymectomy failed to relieve the pain. Renewed examination 2 years later revealed a small right-sided hernia and extreme tenderness in the inguinal region.

Surgical removal of the vas deferens which was affected with chronic inflammatory changes and which adhered broadly and firmly to the parietal peritoneum in the internal annulus inguinalis.

Relief of symptoms.

Case 2. A male, aged 75, who in February 1948 began to have pain in the left upper jaw. The pain had the character of toothache arising from one of the innermost molars. A dentist found that the pain could hardly be due to a dental disease (X-ray was negative), but removed + 7 which was found to be normal. The pain continued in the same site and increased in intensity. It was gnawing and without attacks of exacerbation. No radiation. No headache. At the hospital of his home-town the patient was given local injections (etocain?) in the belief that he was suffering from trigeminal neuralgia, but without effect. He entered Serafimerlasarettet in Oct. 1948. During the last months he had been sleeping badly because of the intensive pains and had grown ever more irritable and nervous.

On admission the patient appeared to have very severe pain. He exhibited a slight left-sided pharyngeal paresis with distinct rideau phenomena. Slight paresis of the soft palate on the left side. No other neurological signs. Wassermann reaction negative. Afebrile. S.R. 12. X-ray of the skull negative.

X-ray evidence of marked mucosal thickening in both maxillary antra, leaving only a nut-sized cavity medially and ventrally in the left antrum. In the right antrum the thickening was at the bottom, occupying half the cavity. No other X-ray signs.

Puncture and rinsing of the maxillary antra yielded no pus!

As the thickening of the mucosa was more marked on the left side and in spite of the fact that no osseous changes were demonstrable, although the symptoms were of about 8 months' standing, the patient was transferred to the Ear, Nose, and Throat Department of Karolinska Sjukhuset with the diagnosis of an abscess or tumour at the bottom of the left maxillary antrum.

At Karolinska Sjukhuset X-ray examination also revealed thickening of the mucosa in both maxillary antra without evidence of involvement of the bone. X-ray of the teeth in the left upper jaw: A rather marked horizontal atrophy of the alveolar process, leaving the necks of the teeth exposed to a certain extent. There was no evidence of circumscribed apical changes, but the pulp was on the whole strikingly narrow. In other words, X-ray revealed parodontosis.

Operation on Nov. 6, 1948 (Professor Torsten Skoog): *Trephining of the left maxillary antrum, opening of a submucous abscess and curettage of the mucosa.* In an attempt to find the cause of the severe pain, the left maxillary antrum was trephined from the canine fossa, although X-ray had failed to reveal any sign of osteitis in the alveolar process on the left side except a cushion-shaped swelling of the mucosa at the bottom of the antrum. The soft parts were incised over the canine fossa as far as the bone which was exposed in the usual way and the thin antral wall opened with a chisel. The antrum proved to be thin and the *mucous membrane* towards the orbit and on the *medial antral wall* was *thin and delicate with no foreign matter. In the bottom of the antrum there was a projecting oedematous mucosal swelling about the size of a walnut.* When pressed it suddenly yielded *thick pus*. It proved to be a case of a *rather large submucous abscess* situated above + 6 and + 5. At the bottom of the abscess the bone was exposed and somewhat frayed. The pus was evacuated, the mucosa covering the abscess removed for histological examination. The bone at the bottom of the antrum was curetted. There was no evidence of communication to any alveolus, and no roots of teeth projected into the antrum. Presumably the inflammatory process originated from the previously extracted tooth, and if there has been a fistula, it must have healed after the extraction. The site was powdered with marfanil, and as there was an opening, as wide as a pencil, doubtless an accessory foramen to the inferior nasal fossa, the antrum was closed primarily without establishing a permanent opening to the nasal cavity.

Microscopical diagnosis (Hultquist): The specimens of mucosa from the respiratory tract show moderate chronic inflammatory changes as well as oedematous and myxomatous transformation of the connective tissue.

Nov. 23rd: The neuralgic pain had almost ceased and the patient was discharged. Later he reported that he remained symptomless.

Discussion: In this case there was gnawing, constant pain which gradually increased in intensity. The absence of attacks of exacerbation spoke against the diagnosis of trigeminal neuralgia, and the symptoms were more suggestive of an inflammatory process under pressure. However, the absence of X-ray evidence of osteitis after the process had lasted for almost 8 months spoke against the latter diagnosis, and the same applies to the negative rinsing of the antrum. The mild left-sided pharyngeal paresis could not be correlated with the pain (beginning bulbar paralysis?). On account of the violence of the pain and the fact that the swelling was more marked on the left side, it was, however, decided to perform surgical exploration.

Summary of the Case: A male, aged 75, with a history of pain of 8 months' standing of a gnawing, constant character. The pain gradually increased, and during the last few months it had been intolerable, disturbing the patient's sleep. X-ray showed mucosal swelling in both maxillary antra, but rinsing was negative. *There were no X-ray signs of bone changes.* On account of the character of the pain and the fact that the mucosal swelling was most marked on the affected side, surgical exploration was decided upon. It showed an abscess, *as large as a walnut*, at the bottom of the antrum. Relief of symptoms.

In both cases surgical exploration elucidated and relieved long-standing painful conditions.

The question as to whether, when, and how the operation should be done is one of many aspects. One does not infrequently come across a morbid desire for operation in which surgical interventions are contra-indicated. It seems to me, however, that in every case of severe and obscure pain, the last method of examination, surgical exploration, is worthy of serious consideration.

SUMMARY

In connection with 2 cases of long-standing, severe, obscure pain (chronic deferentitis with attacks resembling ureteral colic and chronic maxillary abscess without X-ray signs of osteitis), the writer emphasizes the value of surgical exploration, if a complete and accurate clinical examination has failed to elucidate the genesis of the pain.

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**Cerebral Herniations, their Influence
upon Radiographic Pictures, Ventriculography
and Arteriography.
A few Anatomical Specimens**

By

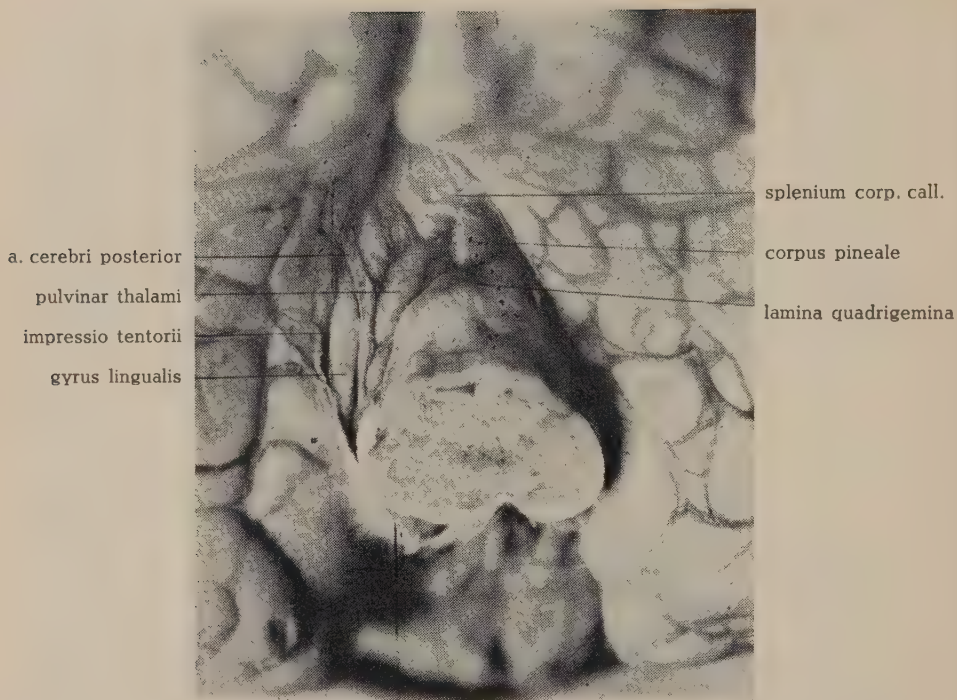
NILS ANTONI

COMMENTS ON THE PICTURES

(The diagrams are all drawn from photographs)

Ad 1-2. Glioma of the left lower parietal lobe. Pineal body strongly displaced to the right. In accordance with a suggestion of *Lilja* (1948), this displacement is brought about by a temporal pressure cone. The cone is built up, in this case, however, not by temporal lobe substance only, but also by the pulvinar thalami. A displacement of the pulvinar into the posterior fossa, below the edge of the tentorium cerebelli, as here, must be especially able to bring about a marked "pineal shift" to the opposite side; displaced parts of the uncinate and lingual region alone attack a little more caudally. In these pictures the arteria cerebri is seen passing in a shallow groove between the temporal pressure cone, s.s., and the pulvinar.

Ad 3-4. Two cases of intracerebral gliomas, in the lower parietal and outer temporal region, respectively. In both, despite the marked difference in the horizontal level of the two growths, the typical deformation of *Winkelbauer* is established: the homolateral gyrus cinguli pushed under the edge of the falx cerebri to the opposite side, corpus callosum slanting, cella media depressed.



uncus *Fig. 1.*

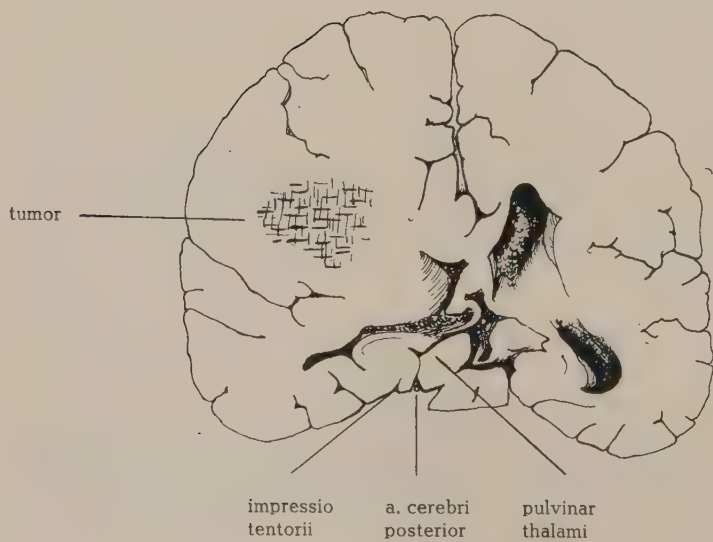


Fig. 2.

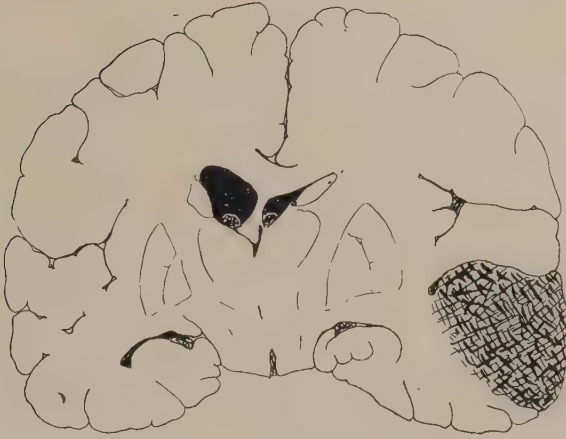
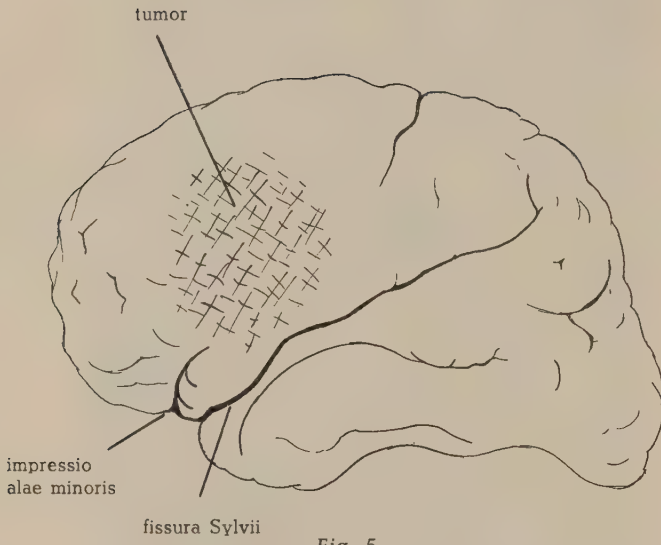
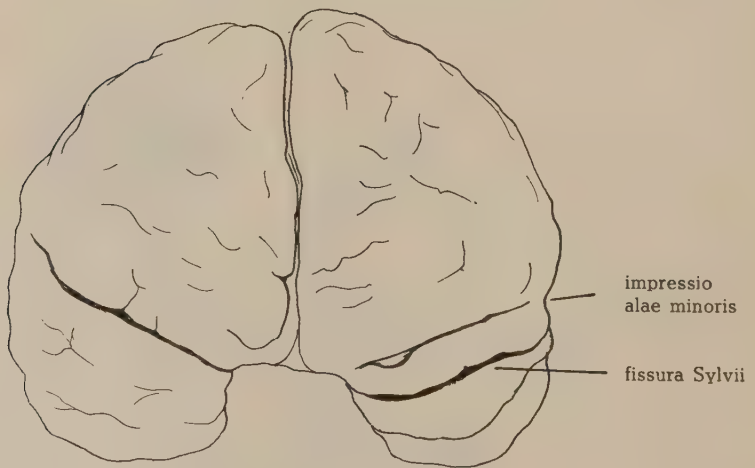
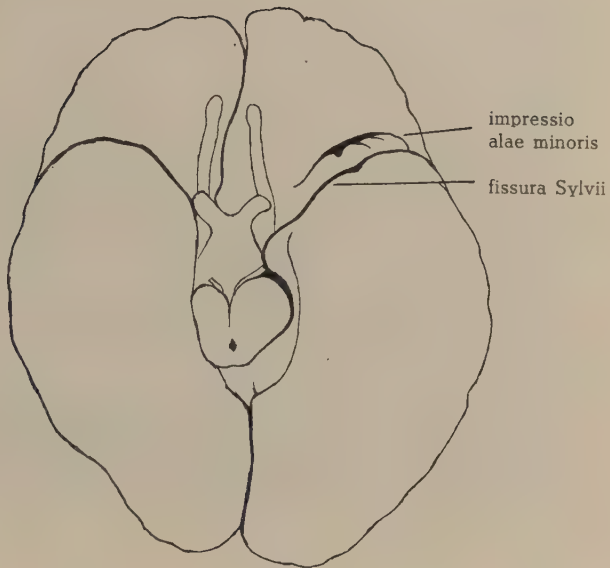
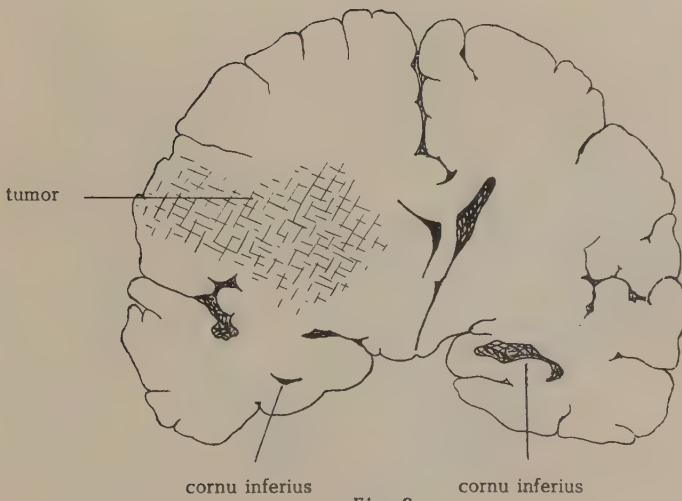


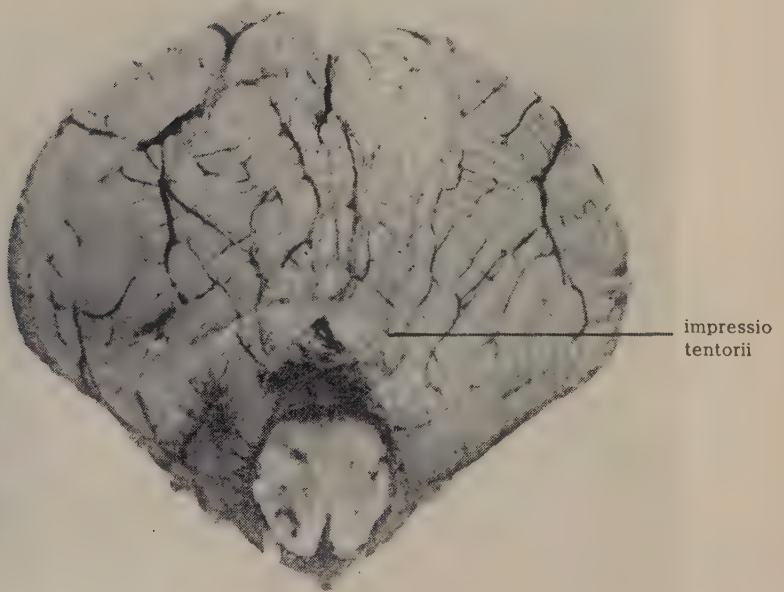
Fig. 3.



Fig. 4.

*Fig. 5.**Fig. 6.*

*Fig. 7.**Fig. 8.*

*Fig. 9.**Fig. 10.*

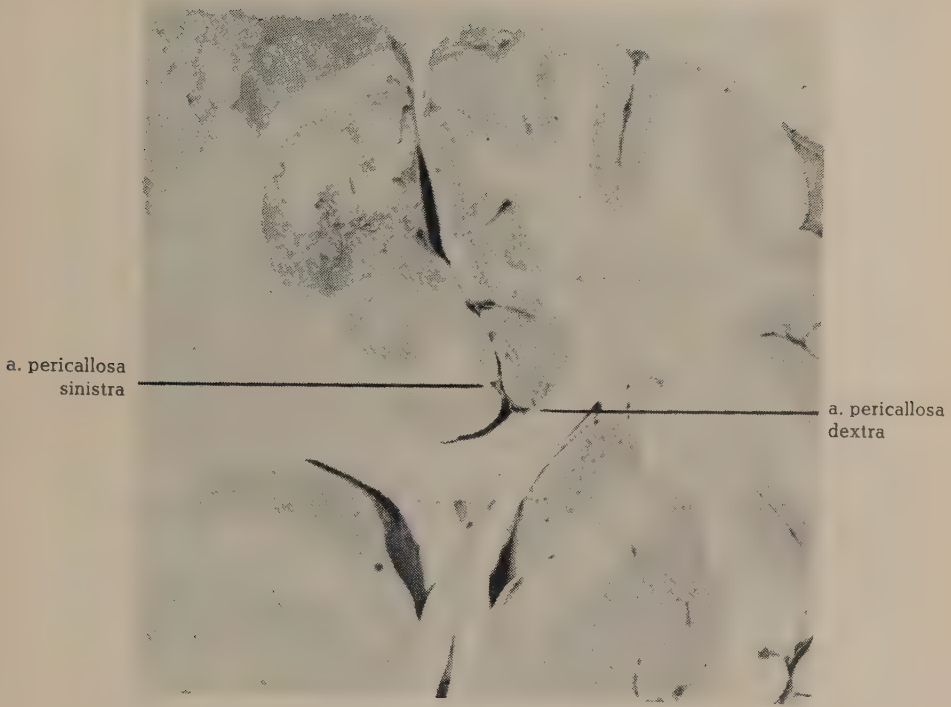


Fig. 11.

Ad 5-9. Glioma of the left frontal lobe. Basal parts of the lobe pushed down into the fossa media by the edge of the ala minor ossis sphenoidalis. Rudiments of such a state were known long ago as an anatomical variant (Giacomini, Eberstaller; Retzius 1896 p. 97), when the edge of the ala minor did not fit properly to the "truncus fissurae Sylvii" (Eberstaller; "vallecula Sylvii" Schwalbe). In such specimens a falciform *impressio alae minoris* is to be seen on the post-orbital surface of the frontal lobe. (A marked *limen frontale valleculae Sylvii* is, in my experience, a constant anatomical element, independent of a possible *impressio orbitalis alae minoris* (Fig. 9)). Displacements of brain substance by the ala minor were, in brain tumors, described by Riessner a. Zülch in 1939, above all when upper parts of the temporal lobe were pushed upward into the anterior fossa. In an actual case, through a real herniation of frontal lobe substance into the middle

fossa, the temporal lobe with its cornu inferius is pushed backwards and depressed.

Ad 10. Lysholm, in 1935, described a characteristic *bayonet deformation* of the aquaeductus Sylvii in cases of cerebellar tumor. Fig. 10 shows such an *upper cerebellar herniation*, first announced in 1939 by *Pichler*, which, in my opinion, causes the Lysholm deformity: rostral cerebellar substance, pushed forwards through the incisura tentorii, presses the posterior part of the aquaeductus Sylvii down, and so brings about the bayonet shape.

Ad 11. Glioma lobi frontalis sinistri. Gyrus cinguli, pushed under the edge of the falx, lifts the arteria pericallosa from the surface of the corpus callosum a few millimeters upward.

The edge of the falx cerebri, as of the tentorium cerebelli, do by no means call forth the displacement of brain substance in case of tumor, but work determining on the degree of displacement in a certain direction.

The matters of fact here represented, seems worthy of a more extensive study.

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Dyskinesia of the Biliary Tract Treated by Bilateral Thoracal Sympathectomy

By

C. FR. BISGAARD-FRANTZEN

Persistence of symptoms following cholecystectomy is the most serious clinical problem in modern surgery of the biliary tract. Many investigations have been carried out to find the cause of the persistent pains and many suggestions have been offered as to the treatment.

In a certain number of these patients pathological changes responsible for the failure of the cholecystectomy can be demonstrated. Prominent among such causes are remaining stones in the biliary tract, residual biliary tract infection and pancreatitis. Stricture of the common bile duct caused by traumatic injury during the operation, or by the passing of gallstones may also explain residual pain.

One of the most common explanations used for the persistence of biliary colic is that of peritoneal adhesions resulting in distortion of the duodenum or the pyloric region of the stomach to the gallbladder bed, or more directly resulting in kinking of the common hepatic duct.

A peptic ulcer can be an origin of attacks of pain resembling biliary colic. Not only can the pains from a peptic ulcer appear like biliary colic, but there is evidence that peptic ulcer may be the origin of functional disturbances in the visceral nervous system associated with biliary colic. (Mallet-Guy, Blandet and Moyson, 1.)

When the causes mentioned have been taken into consideration there still remains a considerable group of patients in which careful review of the whole history fails to give an adequate explanation of the insufficiency of the operation. Such patients are said to suffer from biliary dyskinesia. Though many suggestions have been proposed, the origin of biliary dyskinesia still remains unexplained.

Schrager and Ivy (2) have demonstrated that colic pain can be produced from the biliary tract in dogs by distension of the gallbladder and the biliary ducts. Zollinger (3) has shown the same mechanism of pain in man.

Also Zollinger and Walter (4) and Bronson Ray and Neill (5) have found that typical biliary colic can be elicited by distension of the gallbladder and the biliary tract, manipulation, traction and faradic stimulation of the extrahepatic biliary tract. The pains produced were associated with nausea and vomiting.

Biliary pain caused by stones in the tract is thought to be produced from distension and increased intrabiliary pressure following intermittent spastic contraction of the smooth muscles in order to overcome the obstruction in the biliary passage.

By biliary dyskinesia the origin of the pain is not clearly established but it is most likely that the pains are produced from principally the same mechanism as by gallstone, namely by increased intracholedochal pressure associated with distension. This mechanism of the pain has been suggested by most authors studying the post-cholecystectomy syndrome (1, 6, 7, 8, 9, 10, 11, 12).

Normally, contraction of the gallbladder and the common bile duct is associated with relaxation of the sphincter of Oddi. Increased intracholedochal pressure in a biliary tract free from stones can only be produced by disorganization of this mechanism resulting in contraction of the muscular wall without simultaneous relaxation of the sphincter of Oddi. According to Ray and Neill (5) pain from the gallbladder will result when it is distended at 550 mm water. The tone of the sphincter of Oddi in man has been

estimated to between 55 mm and 680 mm water. (Doubilet and Colp 13, Oddi 14, Elman and Master 15). From these figures it appears that pain may result if the functional correlation between the muscular wall and the sphincter of Oddi is disturbed.

The importance of the spasm in the sphincter of Oddi for the origin of dyskinesia of the biliary tract is proved by the clinical experience that attacks of dyskinesia can be relieved by amyl-nitrite and nitroglycerine (Lagerløf 16, Vachou and Blandet 17), which is known to result in relaxation of the sphincter of Oddi. Otherwise it is generally known that morphine which produces contraction of the sphincter can cause an attack of pain (Lagerløf 18).

Westphal (19) in guinea-pigs found that with moderat electrical stimulation of the vagus nerve below the diaphragm contraction of the gallbladder was produced together with peristaltic movements in the antral portion of the sphincter of Oddi and relaxation of the papilla of Vater. With a slightly stronger current contraction of the gallbladder was greater and peristaltic movements of the ampulla were also increased. When a strong current was used, it resulted in violent contraction of the gallbladder combined with a spasm of the antral sphincter.

This is thought to be the mechanism in dyskinesia of the biliary tract. According to Westphal this condition is named the hyperkinetic form of dyskinesia. It is however a question of discussion whether the condition described is not produced by an unphysiological stimulus. Westphal also found that stimulation of the splanchnic nerve caused relaxation of the gallbladder and the antral portion of the sphincter and contraction of the sphincter of the papilla. Transcision of the splanchnic nerve may produce relaxation of the sphincter of the papilla and contraction of the gallbladder and the antral part of the sphincter by relative overactivity of the vagus nerve.

In man Leriche (20) observed that local anæsthesia of the right splanchnic nerve was followed by contraction of the gallbladder and relaxation of the sphincter of Oddi.

It may be presumed that dyskinesia of the biliary tract is caused by a functional disturbance in the nervous regulation of the biliary tract probably by overactivity of the sympathetic nerves or perhaps by overactivity of the vagus nerves. Westphal called the two mechanisms the atonic form of dyskinesia and the hyperkinetic form respectively.

Segal, Friedman and Watson (21) claim that dyskinesia of the biliary tract is commonly observed in highly nervous, irritable type of patients. They assume that dyskinesia is a functional disturbance resulting from psychogenic factors comparable to those responsible for pylerospasm or cardiospasm, intrinsic gallbladder disease, and reflex disturbances from diseases in other gastro-intestinal organs. The nervous irritable mental state of the patients suffering from dyskinesia often results in the suspicion of hysteria or drug addiction.

The diagnosis of dyskinesia is usually not established until cholecystectomy without relief has been carried out and no anatomical pathological condition in the biliary tract responsible for the persistence of symptoms has been found. Therefore many authors have suggested that the loss of the gallbladder function is the real cause of the symptoms, and many investigations have been carried out to prove this suggestion.

The frequent dilatation of the choledochus following cholecystectomy has been of special interest for this suggestion. The explanation of this dilatation is not clear. The most common one offered is that the water-absorbing mechanism of the gallbladder is lost at operation. This is thought to increase the pressure in the bile duct resulting in dilatation of the choledochus and in dyskinesia. There is, however, no close correlation between dyskinesia and dilatation of the bile tract, nor between high tone of the sphincter of Oddi and a dilatated choledochus. The tone of the spincter usually has been found to be low after cholecystectomy even when the choledochus is dilated.

The presumption of the writer is that dyskinesia of the biliary

tract is, most likely, not produced by the cholecystectomy but that it has existed before the operation.

This presumption is also supported by the fact that the greatest relief of symptoms is obtained by cholecystectomy when cholecystitis or gallstones are found at operation (Gertz and others 29). In cases where a normal gallbladder was found at operation the symptoms of the patients probably are due to dyskinesia and not to obstruction in the biliary tract.

Since Kappi in 1920 advocated anæsthesia of the coeliac ganglion as regional anæsthesia in operations on abdominal viscera it has been known that the splanchnic nerves transmit pain impulses from the abdominal viscera.

The pathways for visceral pain have been closely studied by Bain, Irwing and Mc Swiney (23) and Balchum and Weaver (24) in animal experiments.

They found that afferent impulses from the stomach and the small intestines are transmitted by the splanchnic nerves and other sympathetic nerves to the spinal cord. The sympathetic afferent fibres enter the spinal cord through the white rami and the dorsal roots. The splanchnic afferent fibres have no synaptic junctions in the dorsal root ganglia nor in the lateral sympathetic ganglia. Afferent impulses from the stomach and the small intestines are conducted to the spinal cord through the white rami from the 4th thoracic to the 3rd lumbar ganglion.

Herrin and Meek (25) observed that the symptoms caused by dilatation of the small intestines disappeared after sympathetic denervation, except anorexia and vomiting which were abolished after transcision of the vagus nerves.

In man Leriche and his pupils (20) have done the basic work in the study of the sensory conduction by the splanchnic nerves and its practical consequences in surgery for relief of intractable gastrointestinal pain (26).

Ray and Neill (5) have investigated the visceral sensation in man, before and after sympathectomy in which the splanchnic nerves and the ganglionated chains were removed from 7th

thoracic to the 3rd lumbar ganglion and observed that extensive loss of visceral sensitivity follows this operation. They found that the extrahepatic ducts possess a bilateral sensory innervation. The gallbladder has probably also bilateral sensory nerve supply. This cannot, however, be proved by these investigations since the sensitivity of the gallbladder was only tested after bilateral sympathectomy. After thoracolumbal sympathectomy in man anorexia, vomiting and hunger pains are not abolished, a fact which corresponds with the observations of Herrin and Meek (25). Following sympathectomy after Peets method the writer has observed loss of sensitivity of the stomach. Pain produced by administration of adrenaline in alcoholic solution, 1 mg. adrenaline in 2 ccm. 35 per cent. alcohol, which before the sympathectomy provoked severe gastric pains like those of peptic ulcer, was after the operation without effect.

According to the facts stated above dyskinesia of the biliary tract should be relieved by bilateral thoracolumbal sympathectomy. Not only will the operation interrupt the afferent nerve fibres conducting pain from the extrahepatic bile ducts to the central nervous system, but it will probably also be a cure of the disorder.

Based on the theory of nervous origin of the dyskinesia Reich (27). Perman (28) and H. Lagerløf (16) have described an operation intending to denervate the papillary region of the choledochus. The operative results obtained, however, were not satisfactory, since the pains were only abolished for a short time, weeks or months, probably because the nervous connections were regenerated. As Leriche states it is necessary by sympathetic nerve resection to resect as centrally as possible. Therefore Mallet Guy and Jaubert de Beaujeu (29) by sectioning the right splanchnic nerve have obtained relief of pain in dyskinesia. The satisfactory results of the operation have on later investigation proved to be lasting. As the operation was carried out only on the right side the authors claim that the good results are due to

a radical treatment of the disorder, as a bilateral denervation would be needed to interrupt all the sensory pathways.

Since 1945 in the neurosurgical department of the University Hospital, Copenhagen, fifteen patients suffering from dyskinesia of the bilateral tract have been treated by bilateral thoracal sympathectomy and splanchnicectomy. The operations were carried out by supradiaphragmatic approach as indicated by Peet in treatment of hypertension.

A reexamination of these patients in 1949 showed that one patient still have biliary colic as before the operation, two patients were without pains until a year after the operation, but complain again of the previous symptoms. One patient has developed a functional neurosis caused of constant pains in the back localized to the cicatrices. She was without biliary pain but still a drug addict. The remaining patients state that they are relieved or almost relieved of their previous symptoms.

In the two patients who developed pains after one year possibly the nerve fibres have regenerated. Four patients state that they now have attacks of nausea instead of the previous attacks of pain. This corresponds with the experimental results indicating that the sensation of nausea is conducted by the vagus nerve. As the white rami to the three upper lumbar ganglions usually transmit afferent impulses from the biliary tract, a complete sensory denervation is not obtained by Peets operation. The one case in which there was no effect of the operation probably belongs to the hyperkinetic group of biliary dyskinesia. Even in the hyperkinetic group relief might be expected by bilateral thoracolumbal sympathectomy.

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Primary Melanoma of the Leptomeninges

By

G. af BJÖRKESTEN

Although *Virchow* already in 1859 reported the first case of primary melanoma of the leptomeninges, this type of tumour is still 90 years later considered very rare. During the last 15 years more comprehensive reviews of the earlier literature supplemented by the authors' own cases have been published: by *Bjørneboe* (1934) 41 cases, *Akelaitis* (1935) 30 cases. *Lenče* (1937) 44 cases, *Schnitker & Ayer* (1938) 31 cases, *Arnvig & Christensen* (1939) 43 cases, *Urbanek* (1943) 52 cases and *Strong* (1947) 37 cases. These reviews deal with 68 different cases. Moreover cases of primary melanoma of the central nervous system have been published by *Mackay & Hurteau* (1942), *Neuberger, Daniels & Draper* (1943), *Cardona* (1947) and *Oliveras de la Riva & Nersi Mora* (1947). Thus, at present there are reports of 72 cases, which in the authors' opinion were primary melanomas arising in the central nervous system.

It is often difficult or even impossible on the basis of published data to decide whether a tumour can be accepted as primary or not. Yet it is evident that quite a number of these 72 cases cannot be ranged with the primary tumours. This applies to several of the cases in *Lenče's* and *Urbanek's* surveys, in which there were either malignant nevi of the skin or a mole had been removed some time previously. Many of the patients displayed pigmented

nevi of an even very considerable extent (*Bjørneboe*) and under such circumstances one cannot with absolute certainty exclude a primary focus in the skin, even if parts of single nevi have been examined. Besides, in a few cases necropsy was not performed.

The greatly varying number of cases in the different surveys is a further index of the difficulty in selecting the certain cases. This is partly due to the fact that the same principles are not applied to the various reports, some authors (*Strong*) only considering decidedly cancerous tumours, whereas others (*Arnvig & Christensen, Urbanek*) also include supposedly benignant cases.

It is characteristic of all the cases, even of those which initially appeared to be benign, that the patients finally expired, the vast majority after a rapid, some after a more delayed course of illness. One patient died after two operations; at the first a primary tumour was extirpated, at the second a recurrent one was removed (*Arnvig & Christensen, Christensen*). This was a case of the very rare circumscript form, most of the cases reported being diffuse.

Case report: L. S., 33 years old sea captain (File no. 74/1948) entered the Neurosurgical Department of Södersjukhuset, Stockholm on January 3, 1948. The patient had been healthy until November 1947 when he felt shooting pain above his right eye when coughing. A fortnight later a feeling of numbness on the right side of the face set in.

The objective examination on admission showed considerable loss of sensation in the area of the fifth nerve of the right side with a very weak corneal reflex and deviation of the lower jaw to the right. The right pupil was somewhat smaller than the left one, otherwise no pathological neurological signs were observed. The eye-grounds were normal as was the spinal fluid, the pressure of which was not increased. Cerebral angiography on the right side showed normal conditions. The encephalography showed the left lateral ventricle to be somewhat larger than the right one but there was no local deformation or shift of the ventricular system. The diagnosis remained uncertain; the possibility of a tumour of the Gasserian ganglion or a small focus in the pons was considered. After discharge on January 10, the patient was readmitted on February 16. The pain in the forehead had abated but the feeling of numbness had increased. The examination now showed a further loss of sensation in the entire right trigeminal area. The right corneal reflex was totally absent. Ophthalmoscopy showed slight blurring of nasal margins of both discs. Renewed angiography showed the same finding as before.

The patient was discharged on February 21, but already the following day a paralysis of the abducent nerve of the right side set in and shortly afterwards severe headache and vomiting. Readmission on March 2. The patient now had incipient papilledema, a total right abducens paralysis and a slight

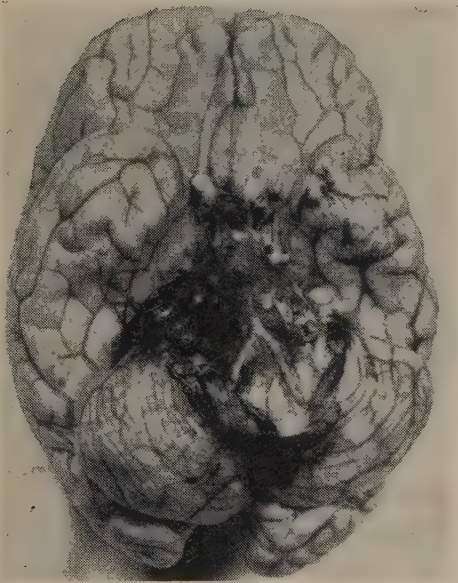


Fig. 1.



Fig. 2.

facial weakness of the left side. During the following days severe headache and left abducens paralysis occurred. Ventriculography on March 8 showed a slight and somewhat asymmetric hydrocephalus, the left lateral ventricle being larger than the right one, but there was no dislocation nor local deformity. A diffuse leptomeningeal tumour was suspected, but the examination of the spinal fluid showed no tumour cells. Yet the suspicion remained and X-ray therapy was begun on March 9. During the following two days there was a

rapid and grave change for the worse with high temperature, severe headache, stiffness of the neck, pain in the lumbar region and legs, apparently total deafness, and paralysis of the pharynx. The pupils did not react to light. There was a total paralysis of the trigeminus on the left side also, the jaw was hanging down. The patient was nearly unconscious.

In the afternoon of March 11 there was a sudden improvement with return of consciousness. The pain in the limbs decreased, but the paralysis of the

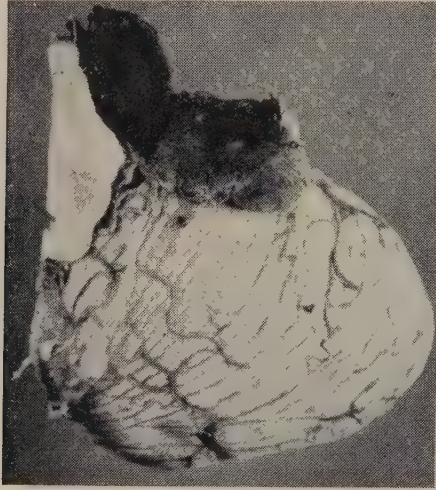


Fig. 3.

pharynx still remained and a paralysis of the vagus with tachycardia occurred. On March 15 there appeared an extreme weakness of the arms but no loss of sensation. On March 17 the patient again felt severe pain in the legs which were almost totally paralyzed. Reflexes of the knee and ankle were bilaterally absent, but sensation was normal. Sensation reappeared partly in the left trigeminal area and the left abducens paralysis abated.

On March 19 the papilledema had increased to 2 diopters. The tachycardia continued and resisted any treatment whatsoever. The paralysis of the pharynx gradually subsided. Improvement continued until April 5. Motility of arms and legs was improved, temperature became normal. Yet the paralysees of the trigeminus and the abducens of the right side remained unaltered.

On April 6 rapid deterioration occurred, with gradual onset of unconsciousness and death on April 10, 1948.

Autopsy on April 12 (F. Wahlgren, M.D.): Positive findings in the body only from lungs, in the posterior lower parts of which there were small fresh pneumonias. Nothing of special interest from heart, the big vessels, ventricle, intestines, liver, bile ducts, pancreas, portal vein, spleen, kidneys, adrenal glands and urinary tract.

Brain: The dura was tightly stretched. On the convexity of the brain the leptomeninges were thin and transcendent. The gyri were flattened and the sulci shallow. On the base of the brain the right cerebellopontile angle was filled with a black, tarry mass in a tumour-like formation the size of a pigeon's egg (Fig. 1). A thin layer of similar black mass was found in the leptomeninges covering the lower and anterior surfaces of the cerebellum. On account of the tumour the right side of the pons showed a slight, cup-shaped impression.

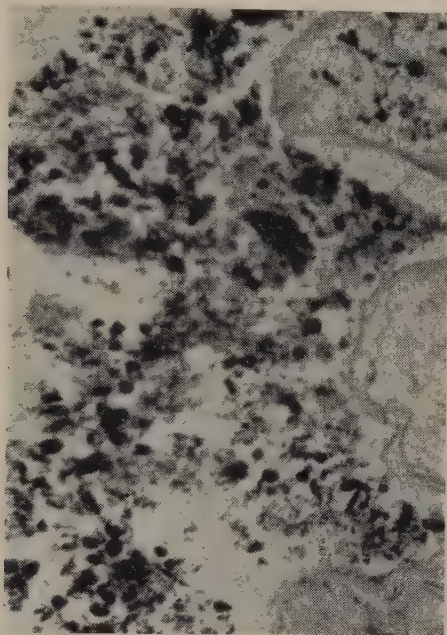


Fig. 4.

Tumor growing in the leptomeninges in the vicinity of the Gasserian ganglion.
Van Gieson stain $\times 80$.

On the posterior surface of the spinal cord, especially in the lower thoracic and lumbar regions, there was a similar layer of brownish black tarry mass in the leptomeninges. The spinal cord displayed no other macroscopically visible changes (Fig. 2).

A cross-cut through the cerebellopontile angle proved the dimensions of the black tumour to be $38 \times 23 \times 20$ mm. The border between the tumour and the somewhat deformed pons was everywhere perfectly distinct (Fig. 3). The thickness of the tumour layer in the lower parts of the spinal cord ranged from 1 to 2 mm. The dark layer could be followed along some of the spinal

¹ The author is indebted to dr. K. E. Svensson for the microphotographs.

roots as far as their exit from the dural sac. There were no signs of ingrowth into brain or spinal cord.

The *microscopy* showed a tumour rich in cells and growing in the leptomeninges. The cells were either round, oval, or polygonal and especially abundant around the blood vessels. Some of the vessels were surrounded by 2 or 3 layers of closely packed cells. Around other vessels the cell arrangements were less pronounced. All the tumour cells contained plenty of brownish

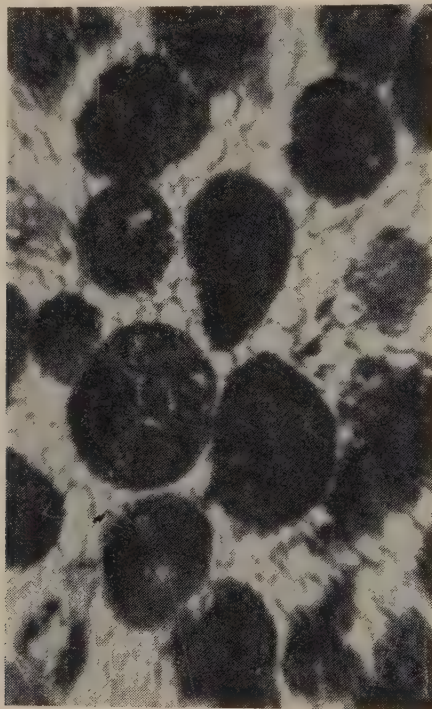


Fig. 5.

Part of the solid tumour in the cerebellopontile angle.

Van Gieson stain $\times 600$.

black pigment. The majority of the cells were so rich in pigment that their structure was not visible, in some the nucleus could be discerned but mitoses could be detected only in a few cells. Comparatively large amounts of pigment were also found outside the cells.

Sections from cranial nerves showed that the tumour infiltration of the leptomeninges continued along the nerves as far as their foramina of exit from the cavity of the skull. In the right ganglion Gasseri the ganglion cells were compressed, forming a thin layer between the dura and the tumour. The tumour cells were less numerous, but the pigmentation of the cells was at least as

intense as in the main tumour. Here, too, there was some extracellular pigment.

The pigment gave no iron reaction, it was decolorized by hydrogen peroxide, and proved to be melanin. Consequently the tumour was a melanoma.

DISCUSSION

This is, undoubtedly, a case of primary melanoma of the central nervous system. No other tumours could be proved on autopsy, there were no nevi in the skin and the repeated eye-ground examinations ruled out the possibility of tumour in the eyes. It appears likely that the primary focus of the tumour was the right cerebellopontile angle. This supposition agrees well with the patient's first clinical symptoms from the right trigeminal nerve. The tumour here, as in most reported cases, extended diffusely. The extension of the tumour in the meninges of the base of the brain agrees well with the normal occurrence of melanin pigment, as described by *Baader*. The pigmentation, however, was much more intense than in most of the cases previously described.

The diagnosis of diffuse leptomenigeal tumours is always difficult. In this case the primary symptoms, mainly limited to one single cranial nerve, rather indicated an infranuclear lesion of the trigeminal pathways of the right side between the pons and the ganglion Gasseri. Already during the second period of hospitalization a diffuse neoplasm on the base of the skull was surmised and when, during the third period, the illness took a serious turn the suspicions gained further ground. According to *Nielsen* the ventricular system in cases of diffuse leptomenigeal neoplasms is either normal or only slightly dilated. The latter was the fact in my case and this seemed further to confirm the diagnosis. Consequently, the spinal fluid was examined with regard to tumour cells, but the result was negative, as in all hitherto published cases of primary melanomas of the central nervous system. In *Loewenberg's* survey of metastatic intracranial melanomas including 85 cases, cells containing melanin were observed only once in the spinal fluid. In my case with its large

tumour masses of a very soft, nearly liquid, consistency it appears most likely that repeated lumbar punctures would finally have led to positive findings. This, of course, is the only means of making an exact clinical diagnosis.

It is noticeable that the intense pains in the limbs were accompanied by pareses without any sensory disturbances. *Schnitker & Ayer*, on the other hand, stated that motor disturbances were the commonest spinal symptoms among their cases, but "the sensory changes were usually of an anesthetic nature rather than pain".

In very few of the hitherto published cases the patients received X-ray treatment. In my case the treatment (4500 r), which was initiated on the mere supposition of a diffuse meningeal tumour, seemed to be of some slight effect, although it could not prevent the illness from ending fatally. Otherwise it is scarcely possible to explain the considerable improvement, appearing about a fortnight after the beginning of the treatment, when most of the previously very pronounced cranial and spinal nerve symptoms receded. Any definite effect is not to be expected, the melanoma being the most radioresistant of all neoplasms (*Baehr*).

SUMMARY

A short survey of the hitherto published cases of primary melanoma arising from the central nervous system is given. The author then describes an additional case. The patient, a 33 year old man, showed symptoms from most of the cranial and spinal nerves. Lumbar puncture showed no tumour cells in the spinal fluid. X-ray treatment caused a transitory improvement but the patient died about 5 months after the first onset of the symptoms. Autopsy showed a diffuse leptomeningeal melanoma, unusually rich in melanin and extending all over the base of the brain and the entire spinal cord.

The author stresses that repeated examinations of the spinal fluid might have led to detection of tumour cells, necessary for

an exact clinical diagnosis. Yet this, of course, would not have altered the prognosis, as the fatal outcome always seems to be inevitable.

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Multiple Cerebellar Angioreticulomas

Discussion of high protein contents of the cysts and of enclosed parts of the subarachnoid space.

By

BENDT BROAGER

Since the description in 1926 by *Arvid Lindau* of the angiomatosis of the central nervous system this disease has been named by the term *Lindau's disease*. It is characterized by hyperplastic capillary angiomas, often cystic, localized to the retina (*von Hippel's disease*) and to the cerebellum, more rarely to the bulb, the spinal cord and different viscera, especially the pancreas and the kidneys. Renal hypernephromas and tumours of the epididymis may be seen. A certain heredity may be observed.

The complete syndrom is very rare, the different components as solitary manifestations being more frequent.

The hereditary occurrence of *Lindau's disease* has been demonstrated through three generations (*Rochat, H. U. Møller, Rumbaur*), and it is observed that the manifestations of the disease may vary in the same family.

From the different reports in the literature bilateral retinal affection seems to be found especially with pronounced hereditary occurrence of *von Hippel's disease*.

Lindau described the tumours as hyperplastic capillary angiomas: The characteristic vessels of the tumour tissue chiefly consist of a single endothelial layer like dilated capillaries. The inter-

vascular tissue in the *common* angiomas consists of nervous tissue more or less degenerated. In the hyperplastic capillary angioma the intervascular tissue shows pseudoxanthomatous cells and small giant cells in direct contact with the "capillary" vessels. The cells of the intervascular tissue rarely show any clearly defined limits and by their mutual connections form a netlike cyncytium (*Lindau* 1926, p. 50).

As stressed by *Roussy & Oberling*, this description of the intercellular components of the intervascular tissue is hardly correct. The endothelial cells, called pseudoxanthomatous as they are mostly filled with droplets of fat, are surrounded by a rich network of reticulin with some collagen in sclerotic areas.

Such a network of reticulin with pseudoxanthomatous endothelial cells is characteristic of the reticulo-endothelial tissue, and *Roussy & Oberling* therefore proposed the term *angioreticuloma* for the hyperplastic capillary angioma of *Lindau*, feeling that this term would better characterize the histological nature of the tumour.

In the Latin countries the term of *Roussy & Oberling* is generally accepted. In Denmark we use the term *angioreticuloma* as it seems to us an exceptionally good term which sums up the two main characteristics of this tumour.—The term *Lindau* tumour is used too.

From the 1.5.34 to 1.4.49 2065 microscopically verified intracranial tumours have been operated upon in this clinic. Out of this series only 33 patients presented cerebellar angioreticulomas, corresponding to a percentage of about 1.6.—It is then a rare tumour.

Multiple cerebellar angioreticulomas are rarer still, especially successfully operated upon. They have been seen partly as simultaneous occurrences found at the same operation (*Levin*), or at autopsy without preceding operation (*Sladden*), partly occurring as single tumours with different localisation at an interval

of several years. (Norlén). Multiple occurrence of angioreticulomas located partly to the cerebellum, the spinal bulb, the medulla oblongata or the spinal cord have been reported several times from post-mortems.

In three patients (out of our 33) multiple occurrence of cerebellar angioreticulomas was observed, the tumours being extirpated with good results and microscopically verified.



Fig. 1.

Case 1. Localisation of midline tumour in 1936, of right lateral tumour in 1945.

Each of the three case histories is curious in some way, as will be related below. The two first cases have formerly been reported on, one of them only in part, by H. U. Møller. The third case was operated upon a short time ago.

Case 1. (H. U. Møller, 1944, case 2) RH. Nk. 508 and 6266, female. At the age of 26 she was admitted for the first time in 1936, pregnant for the second time in the sixth to seventh month. Twelve years earlier failing vision in the left eye and a typical von Hippel's disease had been demonstrated. On account of increasing intraocular pressure with pain and cataract she was operated upon two years later. Left blindness followed. For four months she now had presented symptoms with headache in the neck and the top of the head, especially after movements and turning of the head towards the left, often combined with nausea and vomiting and with typical fits of gyratory vertigo. This dizziness might develop isolatedly on a single turning over in bed, abating when she turned to the right. Increase of symptoms with respiratory difficulties.

Findings: The head is fixedly rotated to the right, flexed to the left side. Right papilloedema of four diopters, left blindness with grey membrane in pupil. Slight paresis of buccal branch of right facial nerve. Positional nystagmus

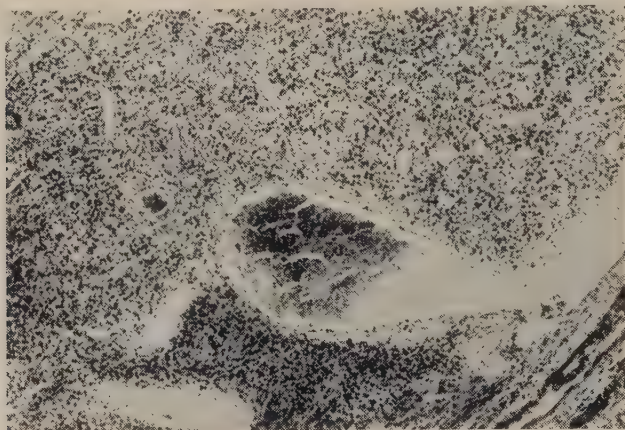


Fig. 2.

and slight left dysdiadochokinesis. Gait was not tried, had been of a cerebellar type. Deep reflexes all feeble, otherwise natural. X-rays showed a thin-walled cranium with abnormal diploic vessels in left posterior fossa.



Fig. 3.

Operation (June 1936. E. Busch): The cystic tumour was situated in the midline with a big cyst in the vermis and a mural tumour the size of a small walnut in the right wall of the cyst (Fig. 1). The mural tumour did not contact

the leptomeninges or the surface of the fourth ventricle. Microscopy was typical of an angioreticuloma (Fig. 2-3). Two and a half months later she had a natural delivery. The child is living, sound. After the operation the symptoms of the patient receded and she felt sound for 8 years (Two years after this operation the left eye was enucleated).

She was readmitted in 1945 after slowly growing headache for some six months, in the last months severe when she was moving the head; exacerbation of headache also when the neck was resting on the pillow. Increasing diffuse weariness. Disturbance of gait.

Findings: Tense, slightly bulging and tender suboccipital decompression. Right papilloedema of three diopters, left anophthalmia. Right dysdiadochokinesis and dysmetria. On the *Romberg* test she would fall backwards and to the left. The gait was slightly of a cerebellar type. Diffuse, slight hypotonus and very feeble deep reflexes.

At the operation (March 1945, E. Busch) a cystic tumour was found laterally in the right cerebellar hemisphere. The mural tumour was the size of a small walnut (Fig. 1). Microscopy showed an angioreticuloma, exactly of the same picture as the tumour extirpated nine years previously. Postoperatively no complication; X-ray treatment was given.

She continued to have some headache, but no dizziness or disturbances of gait reappeared. Two years after the operation she developed a grave mental depression of uncertain etiology, perhaps partly climacterial, partly from fear of recurrence of the intracranial tumour. Two years and six months after the second operation she committed suicide (barbiturates). No autopsy.

Comment.—As the tumour first extirpated was situated exactly in the midline and the second tumour in the most lateral part of the cerebellar hemisphere, it is quite evident that no recurrence of a primary tumour had taken place. At an interval of 9 years the patient had developed two separate cystic angioreticulomas of alike histological pictures, quite differently localized in the cerebellum.

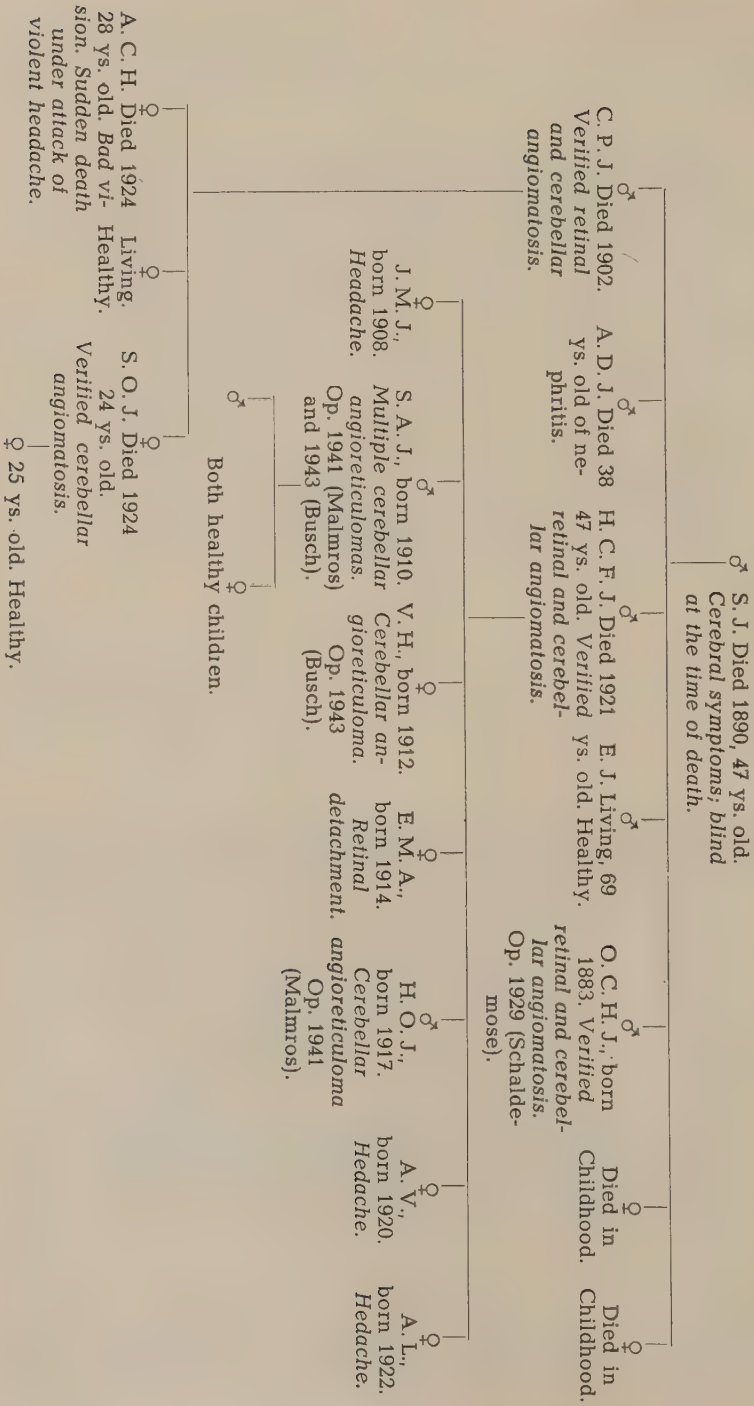
Case 2. (H. U. Møller, 1944, case 5), RH. Nk. 2392, 4367 and 4657. Male, belonging to the *Lindau*-family reported on by H. U. Møller in 1929 and 1944. A copy of the pedigree is given (Fig. 4), no new cases having turned up since 1944.

The patient was 30 years old when admitted for the first time in 1941. For three months he had presented slowly increasing symptoms with fits of pain in the neck and the top of the head, accompanied by dizziness (as if standing on the deck of a ship) and momentary obscurations. The headache was of pressure character and would appear especially on movements of the head.

Fig. 4.

PEDIGREE

(Family of Case 2. From H. U. Møller, 1944).



For two months the natural power in both legs might momentarily disappear; he did not fall, however. For five weeks increasing papilloedema, for two weeks periodical diplopia.

Findings: Bilateral papilloedema of 8 diopters with hemorrhages. Otherwise he presented a normal neurological examination. X-rays were natural.



Fig. 5.

Case 2. Localisation of left tumour in 1941 (Tumour tissue diffusely in walls of cyst), of right tumour in 1943.

Operation (March 1941, R. Malmros): A cystic tumour was found in the lateral part of the left cerebellar hemisphere (Fig. 5). The tumour was subcortical. Microscopy was typical of an angioreticuloma. After the operation he soon felt well, and returned to work.

Two years later he was readmitted as he for three months had developed increasing fits of uncharacteristic headache, especially on sudden movements of the head, nausea and explosive vomiting, and a cerebellar gait. For 6 weeks slight disturbance of the speech and a bad taste in the mouth.

Findings: Bilateral incipient papilloedema. Slight facial paresis on the right side and slight paresis of the right upper extremity, deep reflexes feeble, equal. His speech was dysarthric of a bulbar type. Dysmetria on the pointing test, and dysdiadochokinesis, the side is not specified. The gait was cerebellar; on the *Romberg* test he fell to the right.

At the *operation* (June 1943, E. Busch) no recurrence was seen. In the upper half of the *right* cerebellar hemisphere a big cyst was found almost the size of a tangerine containing yellow fluid (Fig. 5). The mural tumour as big as a cherry was extirpated, and X-ray treatment was given postoperatively. Microscopy gave exactly the same picture as seen in the first tumour.—Examined now, almost six years after the last operation, he is completely sound and able, showing a normal neurological examination.

Comment.—This patient presented two separate angioreticulomas of identical histology at an interval of two years with quite different localisations in the cerebellum.

As seen from the pedigree the family presents in the first two of the known generations four cases of *Lindau's* disease, three of them verified—one very probable. In the third generation four had verified cerebellar angioreticulomas (one of them with multiple occurrence), one had "retinal detachment", one very probably had *Lindau's* disease and three are suffering from headaches. In the fourth generation so far no manifestations of the disease have been observed (the oldest child is 25 years old).

Case 3. RH. Nk. 03223, male, was 30 years old when admitted in 1949. His faculty of vision in the left eye had always been somewhat diminished. Twelve months before admission he had a direct cranial trauma, hitting his forehead against a doorpost. He was unconscious for a few minutes and complained of headache for a few days. For ten months he had slowly increasing fits of headache of pressure-character in the neck and the top of the head. For one month aggravation of symptoms, the headache worse and combined with transitory vertigo of a gyratory type (the surroundings always gyrating from the left to the right). Frequent nausea and vomiting. Decreasing vision, several momentary obscurations and intermittent diplopia with horizontally displaced pictures. For 4 weeks increasing papilloedema. In this department several transitory fits were observed with painful fixation of the head rotated to the right and flexed to the left side; at the same time he would feel very ill, without losing consciousness, however.

Findings: Bilateral papilloedema of 3-4 diopters with several hemorrhages and exudations in both eyegrounds. Vision was normal in the right. 6/18 in the left eye. In the left central fovea some pigmentations were seen, perhaps the result of an old central chorioretinitis. There was a right partial paresis of the sixth cranial nerve with corresponding diplopia. Slight nystagmus when looking to the right. Both upper extremities were hypotonic without any deep reflexes. Slight left dysdiadochokinesis. Slight spasticity of right lower extremity. On admission he would fall to the left side on the *Romberg* test, but reaction was normal the day before operation.

At the operation (Feb. 1949. B. Broager) a cyst measuring 4×4 centimetres was opened in the right cerebellar hemisphere (Fig. 6) and a mural tumour the size of a cherry was extirpated from its localisation subcortically in the tentorial part of the cyst, which contained yellow fluid.—Immediately to the left of the lower half of the vermis a dark red tumour was further observed, only covered by the leptomeninges. It was circular of a diameter of one centi-

metre. At the extirpation this tumour was found to be rather flat with many vascular connections and without the formation of a cyst. Microscopy of both tumours showed the same picture of typical angioreticulomas. Postoperatively his symptoms rapidly receded, and the patient went home feeling well.



Fig. 6.

Case 3. Simultaneous localisations of left, solid, cortical tumour and of right, subcortical, cystical tumour.

Comment.—Some signs had pointed to the right cerebellar hemisphere, some to the left. The simultaneous occurrence of a subcortical cystic tumour and a cortical solid tumour, covered only by the leptomeninges, was interesting and led to some reflections on the formation of cysts in connection with angio-reticulomas of the cerebellum.

Discussion of the cyst.—As the reticular intervascular tissue of an angioreticuloma often shows microcysts Roussy & Oberling believed that the formation of the cyst would start here, perhaps as a xanthomatous degeneration. Increasing in size the cyst would grow outside the tumour which at the operation will be observed as a relatively small mural tumour protruding into the cyst.

Lindau described the site of the tumour to be cortical or subcortical, the tumour often touching the glial membrane.

In our material the mural tumour in most cases was situated without any observed connection with the cerebellar surface or the ependymal wall of the fourth ventricle.

As observed by *Lindau* (1926, p. 112) no cyst will be formed by a small tumour when localized cortically, so that the surface of the tumour may be "drained" into the subarachnoid space.

This was stressed also by *Roussy & Oberling*:—If no drainage takes place to the cerebrospinal fluid on account of the topographical site of the tumour imbedded in the nervous tissue, a cyst is formed. If a tumour is localized to the surface of the cerebellum or a ventricle, no cyst is formed.

One of the cases of *Davidson, Brock & Dyke* was that of a typical angioreticuloma filling the fourth ventricle without any cyst in the surrounding nervous tissue, although the tumour—which was not operated upon—at the post-mortem was found to adhere to a great extent to the walls of the ventricle.

Neither was any cyst found in the case of *Nagliati* with multiple, small, superficial angioreticulomas all over the base of the brain, one in the fourth ventricle and one on the surface of the cerebellum.

Case no. 2 of *Craig, Wagener & Kernohan* is the only one I have been able to find in the literature presenting a cystic angioreticuloma where part of the mural tumour was sure to protrude through the cerebellar cortex. The mural tumour, however, was large and by far the greater part of it protruded into the cyst, as seen in the drawings from the operation.

Case no. 4 of the same authors presented a very large tumour completely filling the fourth ventricle and posterior cistern and involving the pons, the medulla oblongata, and the upper portion of the spinal cord (a cyst was present in the upper part of the cervical cord). Another tumour was imbedded in the right cerebellar hemisphere; it contained a small cyst in the middle.—Perhaps such a small interior cyst later may grow outside the tumour.

The case of *Sladden* showed two small, solid, cerebellar tumours, both superficial, one on the posterior surface of the right hemisphere, the other pedunculated on the lateral surface of the left hemisphere pressed into the cortex by the overlying dura.

The patient was not operated on, the tumours being disclosed at the post-mortem.

The case of *Levin* presented at the operation a cyst in the left cerebellar hemisphere without any visible mural tumour. At the place of the right cerebellar tonsil a solid, vascular tumour was seen. Right below the tonsils a small tumour the size and form as a hazelnut was firmly attached to the posterior surface of the spinal cord. Biopsy from the tonsilar tumour was typical of an angioreticuloma. The tumours were not extirpated. The patient stood the operation well.

In the curious case of *Liebegott* the exact position of the mural tumour is lost to the reader in a wealth of uninteresting details. Two cysts were found, perhaps communicating, one of them protruding into the fourth ventricle, the other into the posterior cistern.

A beautiful illustration of the observation that no cyst is liable to be formed by a superficially localized, small angio-reticuloma is shown also in the third case of this paper.

Most authors who discuss the formation of cysts in connection with angioreticulomas (f.inst. *Lotmar, Keller, Mennenga*) acquiesce in the theory of *Lindau* (1926, 1930), viz.: the result of a transudation from the vessels of the tumour under local or transitory stasis of the vessels.

Hornet, Duperrat & Grepinet, however, believe the cyst to be the result of a liquid secretion by the tumour. If no resorption of the liquid secretion is possible it will expand into and dislocate the surrounding nervous tissue.

It seems to me very possible that a great part of the high protein contents of the cyst may originate in products of degeneration and cell metabolism in the tumour, in short, waste products of the tumour. Anyhow, it is no more speculative than the theory of *Lindau*, perhaps more probable when comparing the contents of the cyst to the contents of the enclosed parts of the sub-arachnoid space seen in some pathological conditions.

High protein values are found in the cerebrospinal fluid of such parts of the subarachnoid space that is cut off from the rest of the space below a spinal block, in the subarachnoid cyst covering a tumour in the cerebellopontine angle regardless of its histological nature, in a cystic arachnoiditis between the cerebral hemispheres or at the optic chiasm,—or the like. It is very seldom seen in cases where the enclosed room is in open contact with the site of production of the cerebrospinal fluid, the choroid plexus, but often with the cortical apertures of the perineural and perivascular spaces of *Virchow-Robin* opening into the enclosed part. The enclosed space may, however, be in contact with the main paths of normal evacuation of cerebrospinal fluid, viz. partly through the arachnoid villi, partly along the spinal roots out into the lymphatics of the spinal nerves.

The cerebrospinal fluid generally is estimated to be completely renewed four times in 24 hours. Perhaps one of the most important functions of the constantly and rather rapidly renewed cerebrospinal fluid is that of evacuation of waste product (and transudations of vessels) from all the surfaces of the central nervous system, no verified lymphatic circulation being present here (the lymphatic vessels of the walls of the bigger intracranial vessels being excepted).

Below a spinal block this supposed evacuation of waste products and products of transudations is stopped with the cessation of the otherwise constant renewal of the cerebrospinal fluid. A rapid rise of the protein values of the closed-off and stagnant fluid is the result.

The generally accepted theory of the high protein values of the fluid being the result mainly of transudations from vessels under local stasis in cases of spinal block, or e.g. from inflamed vessels in cases of subarachnoidal infection, cannot hold true.

Just as high protein values may be seen below an extradural tumour of the cervical spine causing a total block of the subarachnoid space, a syndrome of compression may be demonstrated experimentally. The dural sack may be compressed, e.g.

in a dog after a cervical laminectomy, either by a plug of cotton or by tightening a suture round the dural sack. A typical syndrome of compression will be the result. Neither in the case of spontaneous or of experimental block the subarachnoid vessels will be the site of stasis for more than a short distance, perhaps one or two centimetres. The subarachnoid vessels of the rest of the spinal canal are normal.

As to high protein values in cases with locally inflamed vessels an example may be given, illustrating the importance of waste products of cells.

In regular lumbar punctures in a case of acute meningitis an increase in the number of cells present up to a certain maximum will be observed. A decreasing curve is then seen, and this decreasing curve of the number of cells will be crossed by a rising curve of the protein values of the same spinal fluid.—So the growing destruction of cells, not the healing inflammation of vessels, will be the main cause of the high protein values. It must be stressed of cause, that stagnation of fluid simultaneously may be elicited by a partial, corpuscular blocking of the normal paths of outflow of fluid. (Already in the first observations of *Froin* in 1903 on the syndrome of "coagulation massive et xanthochromie" he found a fluid containing high values of globulin and a great number of cells, at first polynucleated, later mostly lymphocytes, decreasing in number although the globulin did not decrease).

As to high protein values caused by tumours in contact with the cerebrospinal fluid it is known that richly vascular tumours which protrude widely into the subarachnoid space (e.g. big meningiomas on the base of the brain) may be the source of such alterations (*Bligaard*). In these cases the great number of superficial vessels are under local stasis, and possibilities of transudation are great. Tumours with a pronounced tendency to degeneration localized in the subarachnoid space (neurinomas) or protruding into the subarachnoid space (glioblastomas cortical on the base of the brain) may be the constant source of so great quanti-

ties of waste products (rather than transudation substances) that constantly heightened values of protein is the result.

To return to the formation of cysts in connection with the cerebellar angioreticulomas.—Transudation substances from the vessels of the tumour *and* waste products from the special tissue of the tumour *which cannot be evacuated* may explain the formation and increasing size of such a cyst. I believe that the role of the waste products is not to be underestimated.

The pressure of the cyst upon the surrounding nervous tissue may facilitate its growth, as the near-by nervous cells will degenerate on account of hypoxia secondary to the local pressure of the cyst. (Such local degeneration of cells is, of course, partly the cause of the layer of glial reaction observed around almost all growing tumours or cysts imbedded in nervous tissue).

The protein production of a small *cortical* tumour may be evacuated by the passing cerebrospinal fluid so that no cyst is liable to develop.

SUMMARY

Out of a material of 2065 verified intracranial tumours operated upon in the Neurosurgical Department of Rigshospitalet, Copenhagen, cerebellar angioreticulomas were found in 33 patients. Three patients showed multiple occurrence of this tumour and one of them at the operation simultaneously presented a cortical, solid tumour and a subcortical, cystic one.

The formation of cysts in connection with cerebellar angioreticulomas is discussed, and the origin of the high protein contents of the cyst is compared to the origin of high protein values i.a. below a spinal block. Constant evacuation by the cerebrospinal fluid of waste products from all the surfaces of the central nervous system in normal and pathological conditions is thought to be of importance to the non-formation of cysts in connection with superficially localized angioreticulomas of the cerebellum.

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Optimum Mechanical Conditions for the Work of Skeletal Muscle

By

FRITZ BUCHTHAL and E. KAISER

"Elephants do not gallop. They move from places at varying rates of speed. If an elephant wished to catch an express train he could not gallop, but he could catch the train."

Moti Guj-Mutineer. Rudyard Kipling 1891.

The demands made by the organism on its muscular system, and the conditions under which muscular work has to be performed are very varied. The performance of a muscle is determined mainly by three factors:

(1) Its milieu, that is to say, the oxygen tension, the temperature, etc., i.e. factors regulated by the blood supply, and by substances carried in the blood.

(2) The stimulus, i.e. the mechanism which adjusts the muscle's activity to the work by controlling both the number of units which are activated and the frequency of the impulses, the latter being in their turn controlled by the central nervous system, either directly or via impulses from the proprioceptive and other receptors.

Finally, (3) the mechanical conditions under which the muscle must work.

When studying the central nervous system's control of muscular activity, it seemed to be worth while trying to analyse the conditions which are required for the muscle to make an

optimal response to the different demands made on it. The effect of a nerve impulse on a muscle depends largely on the mechanical condition of the muscle at the time, that is to say on its stretch, and on the conditions under which the work must be performed.

Apart from the state of the contractile substance the mechanical reaction depends upon the properties of the mechanical transmission of force between muscle fibres, connective tissues, tendon, and skeleton. It is obvious that variation of the site of attachment of the muscle to the bone and of its line of pull in relation to the latter and thereby of the lever arm can affect the work performed. This has also clinical importance when the forces of different muscle groups are compared, since the ratio between the lever arms of the muscle and of the external load determines the relation between muscle stress and the external load.

Similarly, there are mechanical differences within the muscle's own structure: the units are arranged partly end-to-end in series, so that considerable shortening can be obtained in relation to the length of the whole muscle, and partly side by side in parallel, between two tendon sheaths, so that the tensions of the individual fibres are summated at the expense of the range of shortening.

The investigation discussed here was confined to the study of the active element of muscle, the muscle fibre, under varying conditions.

For this, it is important to know the length of the units at rest, the tension, the shortening velocity required by the organism for the contraction and the rate of relaxation.

METHOD

The apparatus for recording the mechanical response of single fibres must fulfil certain requirements, especially if, as here, it is necessary to measure not only the tension of the fibre, but also the degree and the rate of shortening. When recording a fibre's shortening one may be dealing with rates of up to 10 cm sec^{-1} ,

with accelerations of about 1000 cm sec^{-2} , and with loads between 1 and 1000 dyne, so that the apparatus must be sufficiently sensitive, and must not introduce forces which can distort the true mechanical reaction. Its elasticity, inertia, and frictional resistance must be small in relation to the forces developed within the fibre. For this purpose a myograph has been constructed to make direct photographic records of the changes in a fibre's length; it has a sensitivity of 10μ . Its stiffness is between 8 and 10 dyne cm^{-1} , i.e. it is possible to record a change of load of 0.01 dyne. Its equivalent mass 0.05 g, giving a resonance frequency of 100 c.p.s. with a fibre stiffness of 2×10^4 dyne cm^{-1} . This makes an adjustment period (defined as half the period of an oscillation) of 5 milliseconds. Therefore, it is not possible to obtain an exact record of mechanical changes taking place faster than 5 milliseconds. However, this period is short (0.05-5 per cent.) as compared with the time of a contraction. The damping constant of the apparatus in air is 0.1 (CGS), i.e. several hundred times less than that of the muscle fibre. When the fibre is placed in Ringer's solution the frictional resistance of the apparatus is increased, and amounts to 10 per cent of the resistance of the fibre. The frictional resistance at its highest, i.e. when the shortening velocity is high and the initial load low, amounts to at most 2 per cent. of the fibre's tension.

The movable parts of the apparatus are balanced on a knife-edge suspension, (d, fig. 1) as in an analytical balance, and are moved by a coil (c), which is placed in a magnetic field like the moving coil in a galvanometer system. In order to avoid a directional couple from the terminals of the coil the current is passed in through the mercury cups (e) and (f). The load on the fibre is applied via the lever (a) which is fixed to the moving coil like the needle of a galvanometer. In order to have the greatest possible rigidity with the least inertia the upper part of the lever is triangular, and is made of thin steel tubing to which a hollow glass tube 1.5 mm in diameter is attached. According to whether a constant or alternating current is passed through the coil, the

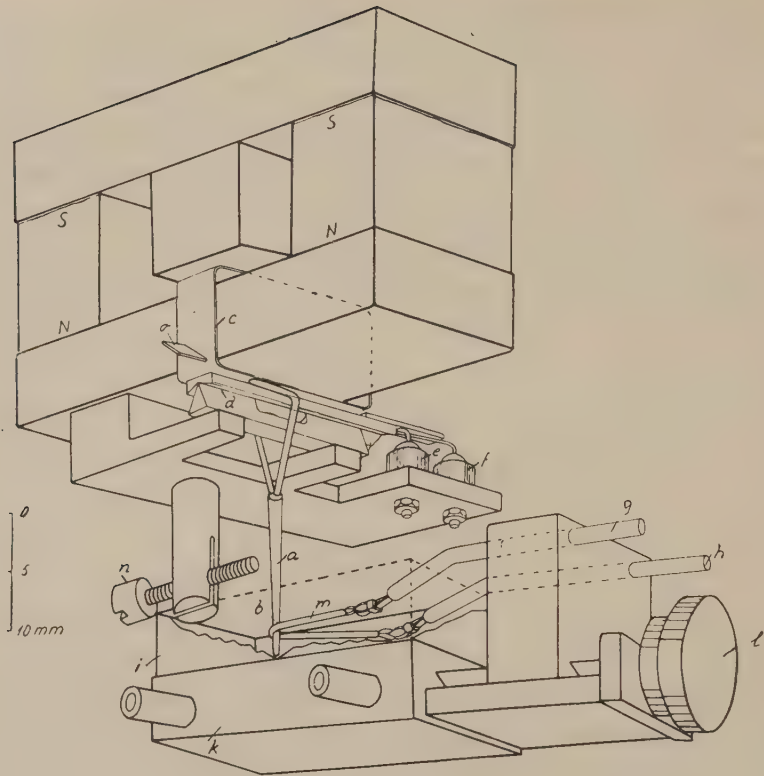


Fig. 1.

Isotonic myograph. m: muscle fibre. a: lever. d: knife-edge suspension. c: moving coil. o: mirror on coil. e and f: mercury cups for transmitting the current to the coil. g and h: silver micro-forceps. l: micrometer screw for varying the degree of stretch. n: adaptable screw for limiting the muscle length (afterload contractions). i: muscle chamber. k: double wall bottom of the muscle chamber.

muscle fibre is submitted to a constant or alternating load proportional to the current. The fibre is attached by its tendon ends between the two pairs of silver forceps (g) and (h), and placed round the lever (a) in the form of a U. In this way one avoids loading the movable part of the apparatus with a clamp for holding the fibre, and also makes it easy to mount the fibre under a microscope without moving the whole apparatus or risking injury to the fibre. This doubling of the muscle fibre, a procedure which does not affect its excitability, contractility, or viability, gives twice the force for the same fibre length and halves the

inertial forces owing to the reduced range of shortening. The fibre is placed in the silver vessel in Ringer's solution and the temperature here is recorded thermoelectrically and varied by running water of a suitable temperature through the double walls (k) of the vessel (i). The length of the fibre is adjusted by the micrometer screw (l), which moves the two pairs of forceps backwards and forwards together. In some cases (for afterload contractions) the length of the fibre is limited by the adjustable screw (n). Movements of the coil, i.e. variations in the length of the fibre, are recorded photographically by optical transmission via the mirror (o). Photoelectric transmission was used for some experiments, and enabled the sensitivity to be increased 20 to 50 times.

The electrical stimulation consisted of rectangular current pulses of variable duration and frequency. The stimuli were either given through forceps (g) and (h) or by a homogenous electrical field parallel to the fibre axis in the Ringer solution. In all cases they were maximal, and their duration and frequency were adapted to give a maximum reaction at the prevailing temperature.

Single fibres and small bundles of fibres from the frog's semitendinosus muscle were used. The fibres running from tendon to tendon were prepared in ice-cold Ringer's solution, containing 6.7 g NaCl, 0.2 g KCl, 0.14 g anhydrous calcium chloride, 0.2 g glucose per litre, and sufficient NaHCO_3 to maintain a constant pH of 7.3 when 99 per cent O_2 and 1 per cent CO_2 is bubbled through. In addition, 3 per cent. dextran was added to maintain a suitable colloid osmotic pressure. The mechanical reactions were studied at different temperatures between 0 and 25° C.

RESULTS

When a muscle fibre contracts in response to a stimulus the response varies with the mechanical conditions. One of the factors determining the optimum effect of a contraction is the length

and tension of the fibre at rest. The length of a muscle fibre, as of other highly elastic substances, e.g. rubber, increases greatly with increasing load. Fig. 2 shows the length-tension diagram of the resting muscle fibre and the curve for the isometric maxima. The latter represents the maximum tension exerted by the fibre during isometric contraction at a given length. In isometric contraction the tension exceeding the resting tension (extra-tension) has its maximum at approximately the fibre's natural length, i.e. its equilibrium length. Isometric "work", which, by definition, occurs without any external change in length corresponds to static work in the organism and the total isometric tension is virtually constant and maximal between the equilibrium length (length $l_0 = 100$) and length 200. At lengths shorter than the equilibrium length the isometric tension decreases rapidly, and reaches zero at about length 60. A single fibre can be stretched over 100 per cent of its equilibrium length, but the corresponding total muscle has only half this extensibility. Certain isolated human muscles also can be stretched by half their equilibrium length, but in most muscles the internal structure is such that the extensibility is considerably less. The best observations on the mechanical behaviour of human muscles were those made by *Ralston et al.* (1947, 1949) on isolated muscles and groups of muscles of amputation stumps in human subjects. However, no information is given on the equilibrium length of the muscles investigated.

Theoretically, the area between the length-tension diagram at rest and the curve of the isometric maxima could be understood to express the net work which the fibre can perform (distance $\times$ force expressed in units l and p , where l is the equilibrium length, i.e. the length for tension zero and P_0 the maximum tension produced in an isometric tetanic contraction). It would require that subsequent release with shortening from isometric contraction should follow the curve for the isometric maxima. This, however, is not so. Even if sufficient time is allowed for complete adjustment of the tension to the new length, the tension on

release is considerably less than the isometric maximum, somewhere halfway between the curve for the isometric maxima and the resting curve. If an isometric tetanic contraction is induced, and the fibre is then allowed to shorten to the same tension as

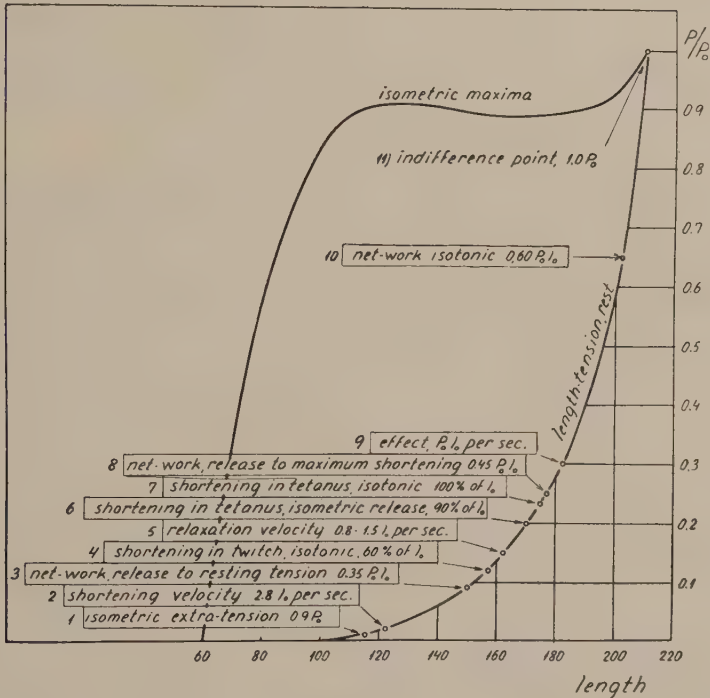


Fig. 2.

Length-tension diagram at rest and during isometric contraction. Optimum values of length and tension for different types of work.

Ordinate: Tension in relative units (P/P_0).

Abscissa: Length in relative units (equilibrium length $l_0 = 100$).

it had at rest, the shortening will vary with different initial lengths and tensions. The length-tension relation which is arrived at by this procedure is termed a *release length-tension diagram*. The maximum shortening occurs with an initial length of 170 (at 0° C.), and amounts to 90 per cent of l_0 (fig. 2 no. 6). If the stimulation is briefly interrupted during the release period it is possible with low release velocities to increase the work up

to 50 per cent. After the interruption the fibre adopts a new and shorter equilibrium length during contraction (*Buchthal, 1942*). The curve for the isotonic maxima obtained by allowing the fibre to shorten in response to tetanic stimulation with different constant loads lies between the release curve and the curve for isometric maxima. It shows that, at length 175 and 0°C ., a maximum shortening of 100 per cent is obtained (fig. 2 no. 7). The maximum for an isotonic twitch lies at about length 160 and presents at 0°C . 60 per cent of the equilibrium length (fig. 2 no. 4).

An account of the optimum working properties of a fibre is not complete if only the *maximum shortening* is considered. Varying the tension and the extra-tension with different degrees of stretch results in different *maximum work* under the various mechanical conditions. The maximum work at a given maximum tension is obtained during a contraction begun *isotonically* and is represented by the area *abcda* in fig. 3. This kind of work corresponds in the living organism to e.g. slow walking, or raising a mass from *a* to *b* with a constant load and a diminishing force in the last part of the contraction from *b* to *c*. The maximum work during such an isotonic contraction (fig. 2 no. 10) occurs at about length 200 and it is difficult to see how this can be attained in the organism. When stretch of the resting muscle is prevented by a stop, the isotonic work during *afterloaded contraction* is diminished. The less the degree of stretch allowed, the more the work is reduced. This type of contraction occurs in the organism when the elongation of the muscle fibre is limited by shunting supporting tissue.

The maximum work in isometric contraction followed by release (*release contraction*) (fig. 2 no. 8, fig. 3 area *ab₁c₁da*) is obtained at about length 180 and amounts to 75 per cent of the maximum isotonic work. At this length the isotonic work has fallen from 0.6 to 0.25, and amounts to only 60 per cent of the maximum isometric release work. Thus, it is obvious that the optimum conditions for obtaining maximum isotonic and maximum isometric-release work are not the same. In the organism

work in release contraction corresponds to that muscular activity which results in the quick acceleration of a mass as in a jump.

If, with a given resting load, one wants to find out how many muscle fibres are required to obtain an optimum amount of work

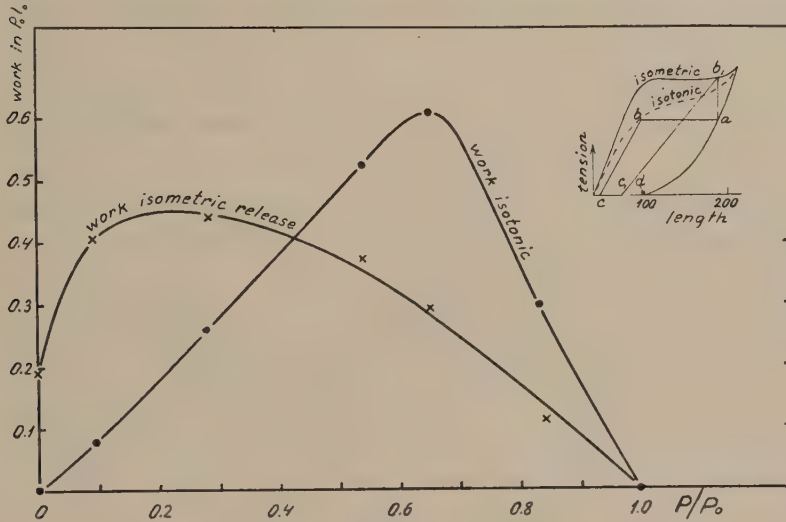


Fig. 3.

Work as a function of the load in isotonic contraction and in release from isometric contraction.

Ordinate: Work in $l_0 \times P_0$.

Abscissa: Initial load at rest, measured in P_0 .

The inset length-tension diagram in the right corner shows the areas for work beginning at the resting point a. The work of isotonic contraction is represented by the area within the points abcd and of release contraction by abcd and a.

during, e.g. isometric release contraction, one can see from the curve in fig. 3 that the fibre performs maximum work at an initial resting load of $0.25 P_0$. The physiological cross-section of the fibre must therefore be of such a size that P_0 is 4 times the given initial tension. If a fibre or set of fibres with a bigger physiological cross-section is loaded with the same absolute load, the relative load decreases and is no longer optimal, which reduces the work produced per unit fibre volume. The optimum resting load for isometric release work corresponds according to fig. 2 to a length of 175.

When the stretch of the total muscle is varied the load is distributed between the connective tissue and the muscle fibres and one of the functions of the more rigid connective tissue might be to keep—in spite of varying loads—the bundles of fibres of different lengths at approximately optimum degrees of stretch. The length-tension diagram of a whole muscle, which has a steeper asymptote than that of a single fibre, illustrates the limiting effect of the connective tissue on the length of the fibres. During *isotonic work*—work with a constant load followed by release, as occurs, e.g. in the muscles of the leg during slow walking with a heavy burden, where acceleration is less important, the maximum work is performed with considerably higher relative loads. Here the optimum is about $0.65 P_0$, corresponding to a length of about 200.

Anything which increases the muscle substance, e.g. training, will cause a deviation from the principle of maximum economy for "normal" requirements. Thus, a muscle with a volume which is 4 times that needed for maximum work in release contraction will only be able to perform 3 times as much work. A fourfold increase of the muscle mass corresponds to a reduction of the relative load to $1/4$. With this reduction of the relative load the relative work performed is reduced from the optimum $0.45 l_0 P_0$ to $0.34 l_0 P_0$, i.e. by 25 per cent.

The work performed by the hypertrophied muscle is graded by a reduction in the number of nervous impulses. Compared with a muscle containing an optimal amount of contractile tissue this involves a loss due to passive deformation of inactive parts of the muscle mass, which in its turn causes a relative increase in the metabolism in proportion to the work performed, and therefore a reduction in efficiency. Similarly untrained muscles perform work less efficiently when the load is small (below optimum load).

This discussion of the optimal conditions for a muscle's work performance has not yet included any consideration of the time factors involved, i.e. the shortening velocity, the rate of release during contraction, and the time for which the contraction is

maintained. It is evident that many of the tasks set to the motor system demand not only a certain amount of work, but also that the work be performed within a certain period of time.

In isotonic contraction the rate of shortening is determined by the load itself (Hill 1938, 1939). In the present investigations

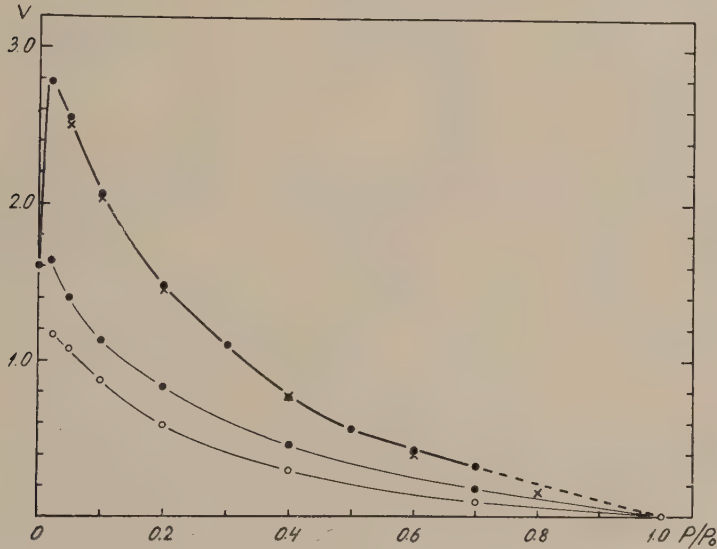


Fig. 4.

Shortening velocity (V , 0° C.) as a function of the load for a single fibre of the semitendinosus muscle (•—•—•), the whole semitendinosus (•-•-•), and the whole sartorius (o—o—o). (Hill, 1939, $a = 0.25 P_0$ and $b = 0.33 l_0$ per sec.).

The points marked as + in the curve for single fibres show the curve calculated according to Hill's equation with constants $a = 0.30 P_0$ and $b = 0.90 l_0$ per sec.).

Ordinate: Relative velocity measured in l_0 per sec.

Abscissa: Relative load measured in P_0 .

the release from isometric contraction was made with the relative velocity which gave the greatest effect (work per unit time). This optimum relative velocity lies at approximately $V = 0.8 l_0$ per sec. (at 0° C.)

Fig. 4 shows the shortening velocity as function of the relative load in isotonic contraction at 0° C. The upper curve represents the mean value for a large number of isolated fibres and small

bundles from the semitendinosus. In contrast to the curve for shortening velocity as function of the load for a whole muscle, which follows the course given by Hill's equation $(P/P_0 + a/P_0)(V/V_0 + b/V_0) = (1 + a/P_0)^1$, single fibres show a maximum shortening velocity at 2 per cent of the maximal load. For the same

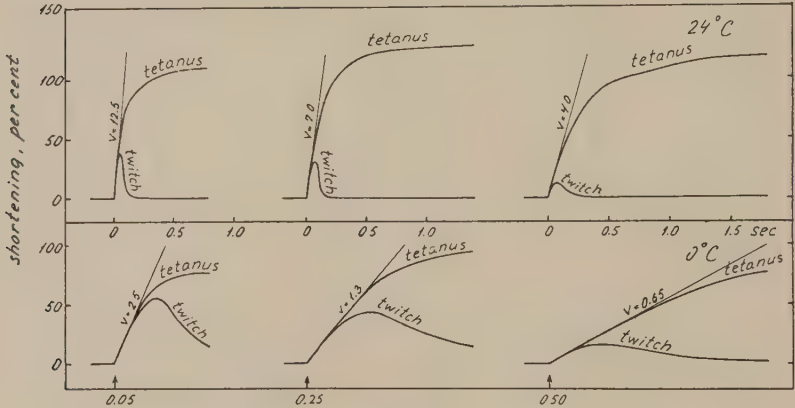


Fig. 5.

The time course of the shortening in single and tetanic contractions with loads corresponding to $P/P_0 = 0.05, 0.25$ and 0.50 at 0° C. and at 24° C. The initial gradient of the curve gives the maximum shortening velocity (V).

Ordinate: Shortening as percentage of equilibrium length.

Abscissa: (In the middle of the figure) Time in seconds.

The lower figures give the three initial loads at rest measured in P_0 .

relative load the shortening velocities of a single fibre are 50 to 70 per cent higher than those of the corresponding whole muscle.

The shortening velocity increases steeply and virtually linearly with increasing temperature between 0 and 25° C. At a low load ($0.15 P_0$) the velocity increases $0.25 l_0$ per sec. per degree C. Fig. 5 shows the course of shortening during a twitch

¹ Where P is the tension and P_0 the maximum in isometric tetanic contraction, V the shortening velocity with load P and V_0 the maximum shortening velocity; a is a constant with the dimension of tension and b a constant with the dimension of velocity. The values of the constants vary for individual muscles.

and a tetanic contraction of the same fibre at 3 different values of P/P_0 and at both 0 and 24° C. The first part of the shortening (maximum shortening velocity) is the same for both a twitch and a tetanic contraction. However, *the shortening* in a twitch diminishes *rapidly* with both increasing load and increasing

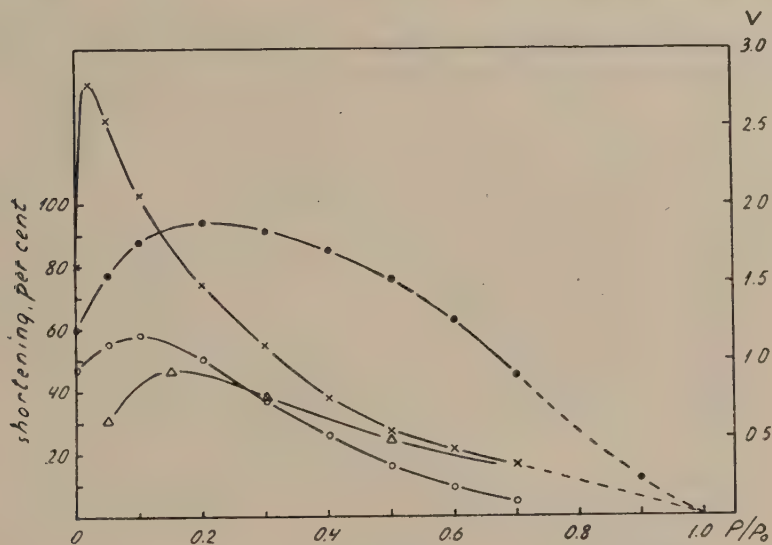


Fig. 6.

Degree of shortening and shortening and relaxation velocities as function of the load.

•—•—• shortening in isotonic tetanic contraction.

o—o—o shortening in isotonic twitch.

Left ordinate: Shortening as percentage of equilibrium length.

x—x—x maximum shortening velocity.

△—△—△ maximum relaxation velocity.

Right ordinate: Relative velocities in % per sec.

Abscissa: Relative load in P_0 .

temperature, while that in tetanic contraction is much less affected by increasing the load, but increases with increasing temperature. This difference between the effects of temperature on a twitch and on a tetanic contraction may be explained by the different effects of the relaxation velocity (fig. 6). In a *tetanic contraction* the relaxation velocity will not be able to affect the maximum shortening, since it does not become apparent until the

stimulus is interrupted. In a twitch also the relaxation begins when the stimulus ends, but here it conflicts with the shortening velocity over the maximum shortening, which occurs when the shortening velocity and the relaxation velocity neutralise each other. Since the relaxation velocity increases about 2-4 times more than the shortening velocity with temperature, increasing temperature will reduce the amplitude of the shortening in a twitch. The different effects of the initial tension on the degree of shortening in a twitch and a tetanic contraction are similarly readily understood. The shortening velocity decreases more rapidly than the relaxation velocity with the tension, and consequently the shortening with big loads falls more rapidly in a twitch than in a tetanic contraction, in which the shortening is not affected by the relaxation velocity. In the transition from a twitch to a tetanic contraction the relaxation velocity will be one of the factors which determines the minimum stimulation frequency required for reaching a certain tetanic level. The lower the rate of relaxation, the lower will be the frequency required. In other words, the impulse rate is most economical at a low rate of relaxation, though the latter must not, of course, conflict with the minimum time required for obtaining alternating muscular activity.

Nature's demands concerning relaxation velocity are very varied. The acceleration forces will cause relatively slow angular movements in large animals and rapid movements in small. This can be illustrated by the following example: Of two similar muscles (a and b) which can perform the same work per weight, a is assumed to have $\frac{1}{10}$ the linear dimensions of b so that the cross-section of a is $\frac{1}{100}$ and its weight $\frac{1}{1000}$ of b's. Each muscle is now required to accelerate a mass of its own weight. Compared with the large muscle b, the small muscle a accelerates a mass of $\frac{1}{1000}$ with $\frac{1}{100}$ of the cross-section of the large muscle. Thus the small muscle can exert relatively 10 times the force and therefore 10 times the acceleration of the large muscle. At the same time the change in length of the smaller muscle is $\frac{1}{10}$ of

that of the large muscle, and it is evident that the work cycle will be completed much more quickly in the small muscle. The frequency (ω) with which a similar movement can be performed is determined by equation

$$\omega = \sqrt{\frac{\gamma}{r}}$$

where γ is the acceleration and r the amplitude of the movement. The acceleration (γ) of muscle a is thus 10 times that of muscle b

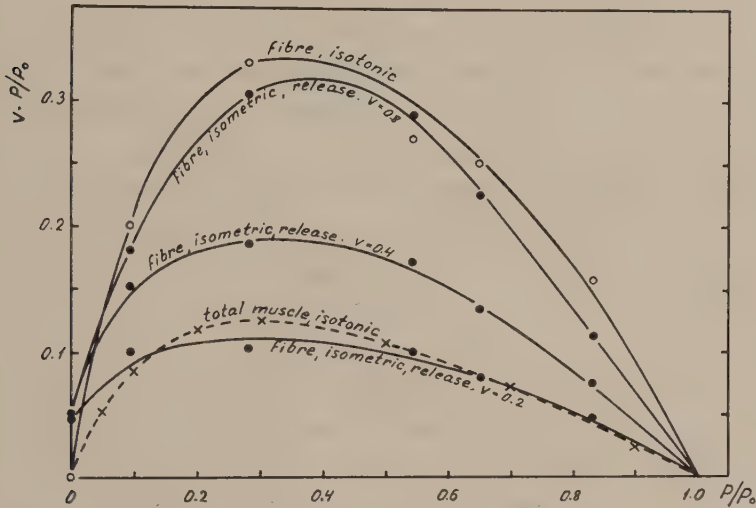


Fig. 7.

Rate of work production as function of the initial load at rest in a single fibre of the semitendinosus during tetanic isotonic release contraction, (release velocities $V = 0.8, 0.4, 0.2$ l_0 per sec.) and in the whole semitendinosus during tetanic isotonic contraction.

Ordinate: Rate of work production expressed in units $l_0 P_0$ per sec. = $V \times P/P_0$.

Abcissa: Relative load in P_0 .

and the amplitude (r) is 10 times smaller than that for muscle b for similar movements with the same ratio between muscular and initial forces. It has already been pointed out that a slower relaxation rate, from the point of view of the number of impulses required, is more economical in the slower movements of larger animals, and that therefore the optimum relaxation velocity must be relatively low. More rapid movements require an increased relaxation velocity at the expense of economy of impulses. The

frequency of muscular action in the wing muscles of insects is up to 200 strokes per second, and, for this, relaxation rates in the order of milliseconds are required, i.e. the relaxation velocity is at least 10 times more rapid than in mammals (Höncke 1947). Assuming the same efficiency and the same cross-section load in insect and mammalian muscles one must expect that insect muscles, which complete twenty work cycles to the mammalian one, will have about 20 times the metabolic exchange per g and per minute. Professor Krogh has measured the metabolic exchange in locusts during flight: he found that the locust's metabolic exchange was about 10 times that of man doing maximum work. As the locust is not a particularly good flier, there is no reason against assuming that values corresponding to those calculated from the mechanics may be attained in other insects.

The maximum effect (e.g. measured in ergs per sec.) of frog muscle fibres is obtained at 0° C. with an initial load of $0.3 P_0$, corresponding to a stretch of 80 per cent (fig. 2 no. 9). If the work is performed isotonicallly the rate of work production is about $0.3 P_0 l_0/\text{sec.}$ (fig. 7). If it is performed from this length (180) by the release of an isometric contraction and with a release velocity¹ of $0.8 l_0$ the same effect is obtained as with isotonic contraction, but with both higher and lower release velocities the rate of work production falls. Figure 7 shows that for all the forms of work which were studied the maximum effect was obtained with an initial load of $0.3 P_0$, corresponding to length 180. This might appear to mean that the whole muscle, which rarely under normal conditions works from a resting length of 180, usually lacks the optimum conditions for a maximum effect. However, the degree of stretch of a whole muscle does not correspond to that of its individual fibres. For fibres arranged in parallel the absolute increase in length is the same for the whole muscle and

¹ The constant release velocities were obtained by attaching the one end of the muscle fibre to a piston moved by hydraulic power transmission and the other to a condenser myograph.

the single fibres. Since the fibres rarely extend over the whole length of the muscle, a given relative stretch of a fibre corresponds to a smaller relative stretch of the muscle. In addition the different lengths of the individual fibres bring about an inhomogeneity of stretch in the whole muscle, which means that one muscle might perform different types of work by selectively innervating the different fibres according to their degree of stretch.

So far we have dealt only with the maximum work and effect in a *single work cycle*. The rate at which work can be performed by alternating muscular activity is naturally affected to a considerable extent by the duration of the period during which no work is done, i.e. during relaxation and passive stretching before the next contraction. Therefore, the mean effect for a whole period (contraction, relaxation and passive stretch) is always less than the absolute effect in the contraction period alone.

DISCUSSION

An investigation of the optimal mechanical conditions for different types of muscular activity shows that for most of them the optimum lies at about a resting length of 150-180. This degree of stretch can be obtained within the muscle in spite of a lower external degree of stretch, by a suitable geometrical arrangement of the fibres. From the point of view of optimum economy for the performance of a given task the results depends on:

1. The type and amount of work to be done.
2. The distance between the ends of the muscle, and the range of absolute shortening.

The minimum amount of muscle substance required is determined by (1) in accordance with the adaptation to optimum effect, which depends on the degrees of tension and stretch at rest (fig. 3).

The geometrical structure of the muscle is determined only by (2). A high tension corresponds to a small range of shortening

and vice versa, and is obtained by grouping the fibres in series or in parallel.

When a constant tension is required at a given length of a muscle it is obtained partly by tension within the muscle substance itself and partly by the connective tissue in parallel with the fibres. If the main function of the muscle is static the most economic performance will be favoured by increasing the connective tissue at the expense of the muscle substance. The reverse may be expected when the muscle has been trained, the more energy-demanding muscle tissue being developed at the expense of the connective tissue (a process which may be considered uneconomical for normal daily requirements). *The conditions under which training* takes place determine the degree of increase in the muscle substance. This is illustrated by changes in the shortening velocity as function of the load. For a given rate of metabolism a runner will run most economically at $\frac{1}{4}$ of his maximum force (P_0) and his muscles will contract during only $\frac{1}{4}$ of the period of a stride. On the other hand a wrestler exerts his maximum tension (P_0) all the time. Since the wrestler's muscles are more powerfully developed than the runner's, though the difference in their metabolism can hardly be expected to be very great, one must presume that tension is the deciding factor in the growth of the muscle's physiological cross-section. This may be important in the effect of voluntary or electrical exercise on denervated or atrophied muscles.

The relation between the muscle substance and the intramuscular connective tissue, as well as the different arrangements of the muscle fibres (in series or in parallel) probably should not be regarded as constant but as variable processes, with continuous competition between the connective and muscle tissues. Looked at from the point of view of the greatest economy it is not unreasonable to assume that for different purposes there is an adaptation of the muscle fibre-connective tissue pattern: work requiring large variations in length favouring an arrangement in series and work requiring small variations an arrangement in

parallel. Comparison of the maximum shortening velocity of a muscle in which the fibres run from tendon to tendon with that of its individual fibres shows that in a whole muscle there is a limiting factor—the connective tissue—which acts as a viscous shunt across the active substance. This restriction on rapid shortening, which considerably reduces the efficiency, is difficult to explain on the principle of the greatest economy, unless the connective tissue is regarded as a factor which can "relieve" the muscle fibres, and helps the muscle to adapt itself to the continuously changing conditions of work.

SUMMARY

The mechanical conditions of single muscle fibres, small bundles of fibres, and corresponding whole muscles have been studied in their relation to tension, shortening, and rates of work. The optimum mechanical conditions of work for a muscle vary according to the task it has to perform.

A myograph has been used to record the mechanical changes taking place with isotonic and isometric contraction. The movable part of the myograph is operated by a moving coil as in a galvanometer, so that the force is exerted electrically. The changes in length are recorded, either optically or by photoelectric transmission.

The optima for the different mechanical functions studied are, for the rate of work production, the work obtained by release from isometric tetanic contraction, isotonic shortening and relaxation velocity in the range of length $l = 150-180$ (0° C.) (equilibrium length = 100). This corresponds to a tension of $0.1-0.3 P_0$, where P_0 represents the maximum tension which can be obtained in isometric tetanic contraction. Only work performed under isotonic conditions has its optimum at a high degree of stretch ($l = 200$, 0° C.), while shortening velocities and isometric extra-tension have their maxima at the equilibrium length or at small degrees of stretch ($l = 100-125$).

The relaxation velocity and its variation by temperature and tension explain the difference between the shortening during a twitch and a tetanic contraction and the opposite behaviours of the shortening with change in temperature. The relaxation velocity changes 2-4 times more with temperature than shortening velocity. The shortening obtained during a twitch is the resultant of the shortening and relaxation velocities, a lower relaxation velocity allowing greater shortening. Similarly a low relaxation velocity allows a low frequency of stimulation for obtaining the tetanic level. On the other hand the low relaxation velocity lowers the optimum frequency of alternating muscle action considerably.

The different mechanical properties of the muscle substance and its interaction with the supporting tissue are discussed in relation to optimum economy.

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Intracranial Carcinomatous Metastases in a Neurosurgical Clinic

By

ERNA CHRISTENSEN

In the Neurosurgical Dep. of the Rigshospital, during the period of June 1934-January 1949 altogether 2023 patients with intracranial tumors were operated on. Microscopic examination has shown the presence of carcinomatous metastases in 82 (*i.e.* 3.9 %) of these cases.

As hitherto no report has been published of a material of metastatic intracranial tumors treated surgically, it seems desirable to investigate which kind of carcinoma most frequently gives intracranial metastases—at a juncture when the general condition of the patients is still so good as to justify the patient being submitted to operative treatment. Furthermore, it is of interest to ascertain whether there is any difference in the character of the metastases in men and in women, whether the different carcinomas metastasize equally early, whether the period of survival after the operation varies for the various metastases, and whether there are any clinical symptoms suggestive of a metastatic intracranial tumor when the primary tumor has given no clinical symptoms.

Finally, in this work an account is also given of the site of the tumors and their histological structure as compared with that of the primary tumor insofar as this is known and examined microscopically.

The material comprises 32 women and 50 men at an average age of 49 and 50, respectively.

Among the women 11 were found to have presented no symptoms of a primary tumor prior to their admission to this department, and in 4 of these patients the primary tumor was not found subsequently either.

Among the 50 men the primary tumor was not verified in 20 because most of these patients died at home, on which account no autopsy was performed. In a few of these cases, however, the autopsy also failed to reveal the site of the primary tumor, a fact indicating, at any rate, that this tumor must have been very small.

The age distribution of the tumor patients is given in Table 1. It will be noticed that all sorts of tumors occur most frequently round the age of 50.

TABLE 1.
Age and Sex Distribution of the Patients, with Location of the Primary Tumors.

	Mam- ma	Ovary, uterus	Lung	Kidney	Pancreas gastro-in- test. can.	Eye, skin	Thyroid	Un- known
<i>Women</i>								
30-39 yrs.	1	1				1		
40-49 "	9	2	2				2	1
50-59 "	2		1	1	1	1		2
60-69 "		1		1	2			1
<i>Men</i>								
30-39 yrs.	1		4		1	1		2
40-49 "			6		1	1		9
50-59 "			8	1				8
60-71 "			3	3				1

From this tabulation it is further evident that there is a decided sex difference, as in 16 out of the 28 women with known primary tumor, this was located in the female genitals (in the breast, in no less than 12 cases) and only 3 women had primary carcinoma of the lung. About half of the tumors (16) occurred at the age of 40-50 years; there were 8 cases in the 6th decade,

while in the 4th and 7th decades there were 3 and 5 cases, respectively. The average age of the women was 49 years.

In the men, carcinoma of the lungs was the form of cancer that most frequently gave intracranial metastases. Thus, among 30 primary tumors established 21 were carcinomas of the lungs. It is also worth mention that in this material there is a case of intracranial metastasis from a mammary carcinoma even though this form of tumor is very rare in men.

As to the age distribution there is no difference between the two sexes, the tumors occurring in men mostly in the 5th and 6th decade, 9 and 7 cases in the 4th and 7th decade, respectively.

One of the patients with metastasis from hypernephroma was 71 years old. The average age for the men is 50 years, that is, almost the same as for the women. If now, instead of the age distribution, we look into the interval between the diagnosis or removal of the primary tumor and the craniotomy with extirpation of the intracranial metastasis, some interesting features are revealed (Table 2).

TABLE 2.
Interval Between the Diagnosis (or Removal) of the Primary Tumor and Craniotomy with Extirpation of the Intracranial Metastasis.

Women	Mam- ma	Uterus, ovary	Lung	Kidney	Pancreas gastro-in- test. can.	Skin, eye	Thyroid	Un- known
In Neurosurg.								
Dep. (autopsy)	1	1	2	1	2			4
< 1 yr.	2	2	1					
1-2 yrs.	1	1		1	1	1	1	
2-3 "	4							
3-4 "	2							
> 4 "	2					1	1	
Men								
In Neurosurg.								
Dep. (autopsy)			16	2	1			20
< 1 yr.			5					
1-2 yrs.	1				1	1		
2-3 "								
3-4 "								
> 4 "				2		1		

Thus, from Table 2 it is evident that the juncture for the metastasis of the mammary carcinomas is incalculable. In the present material they have appeared most often in the third year after the operation, whereas uterine and ovarian carcinomas were found to metastasize at the latest in the second year after the operation for the primary tumor; and the tumors of the lung—in men and women—metastasized within the first year, the metastases here constituting often the first clinical symptom of the primary tumor. Further, it is to be pointed out that malignant tumors such as hypernephroma and melanoma in some cases give intracranial metastases as late as more than 4 years after the operation. The same applies to a case of malignant adenoma of the thyroid.

As to their localization, the metastases show no particular feature. In the women 12 were located on the left side, 14 on the right side, and 6 in the midline. Altogether 9 of the tumors were infratentorial, 1 extracerebral. They were distributed evenly on all the regions of the brain, affecting mostly the cortex. Only in one case did the operation reveal multiple tumors, while on autopsy 3 additional instances of multiple intracranial metastases were demonstrated.

Something similar applies to the men, as here the tumors were located on the left side in 18 cases, on the right in 21 cases, and in the midline in 4 cases; finally the metastases were multiple in 7 cases. Of these tumors only 3 were infratentorial, 3 extracerebral. Here, too, the tumors were distributed evenly on the different parts of the brain.

It is worth notice that in 11 women and 40 men—or 62 % of the total material of 82 cases—the intracranial metastasis has been the first clinical symptom of carcinoma.

The clinical symptoms in these patients do not deviate from the clinical symptoms of primary intracranial tumors of the same localization.

The duration of the illness prior to hospitalization varies from 10 days to 9 months in the women, from 1 week to 12 months in

the men, averaging respectively 3.7 and 3.8 months. In the women the duration of the present illness was less than 3 months in 16, between 3 and 6 months in 8, and between 8 and 9 months in 8. Among the men, 32 had had symptoms less than 3 months, 12 from 3 to 6 months, and only 6 between 6 and 12 months.

Altogether 26 out of 32 women, and 36 out of 50 men, entered the Neurosurgical Department with symptoms of increased intracranial pressure.

It is generally considered that patients with metastasizing carcinoma show a greatly increased sedimentation rate. It is found, however, that this phenomenon is so variable that it affords no reliable evidence of the possibility of a metastatic intracranial tumor. For in the women of this material the sedimentation rate was found to vary between 3 and 115 mm./1 hour, with an average of 32; in the men it varied between 1 and 95 mm./1 hour, with an average of 20.

Considering the time of survival after the operation and looking into the question whether some of these patients became able to work for some length of time before generalized metastasis took place, we find that 8 of the female patients died in connection with the operation. Autopsy was performed in 6 of these cases; and 5 of them showed metastases to the lung besides metastases to other organs. This generalized metastasis explains why the patient could not stand the operation. In one patient no primary tumor could be found on autopsy; here the metastasis was a carcinoma papilliferum. One patient on whom autopsy was not performed had been operated on in a surgical department six months before for a granulosa-cell tumor of the left ovary, and the intracranial metastasis showed the same histological picture. In the other of the two patients not examined post mortem the presence of a kidney tumor had been demonstrated, and the intracranial metastasis was that of a hypernephroma. For 22 patients the average survival lasted 6.8 months, varying from 14 days to 30 months. Two patients could not be traced for reexamination.

Of the male patients 19 died in connection with the operation. Autopsy revealed carcinoma of the lung in 9 of these patients, hypernephroma in 1, and a tumor of the pancreas in 1. None of these 11 patients had shown any clinical sign of the primary tumor. In 3 cases no primary tumor could be found on autopsy; here the intracranial metastases showed respectively papilliferous carcinoma, solid carcinoma, and adenomatous carcinoma.

One patient had been operated on 18 months before for cancer of the breast, and the intracranial metastasis presented the same picture as the primary tumor; no other metastases were found nor any recurrence of the tumor in loco.

Autopsy was not performed on 4 of the patients, and none of these had had any symptoms of a primary tumor. Here the intracranial tumors were found respectively to be metastases of hypernephroma, solid carcinoma, adenomatous carcinoma, and papilliferous carcinoma.

Of the remaining 31 male patients 29 had an average postoperative lifetime of 8 months, varying from 2 weeks to 12 months, while 2 are living at this writing, respectively 6 months and 3 years after the operation. The last case is that of a man who 9 years before admission to this clinic had submitted to left nephrectomy for hypernephroma, and histological examination of the removed intracranial tumor showed also the typical picture of hypernephroma. According to a statement made by his physician, this man is completely free from symptoms and fully able to work. In the first case of these 2 living patients no primary tumor could be demonstrated, but histological examination of the intracranial tumor showed a hypernephroma here, too. The private physician of this patient states that since the operation—about 6 months ago—no new symptoms of intracranial metastases have appeared, but the right inguinal glands were enlarged, and roentgenography of the pelvic bones showed numerous metastases here.

Several of the patients with a relatively long postoperative lifetime have been able to resume their work for a rather short

period. It is an exceptional instance, however, when one man remains capable of work and free from symptoms as long as 3 years after the operation for the intracranial metastasis.

In those cases where it has been possible histologically to compare the primary tumor and the intracranial metastasis, the latter has not deviated in appearance from the former.

Macroscopically the intracranial metastases are well-defined but without any true capsule. Many of them contain degenerative cysts, which in some cases are so large that the tumor has the appearance of a cyst, and where only the microscopic examination reveals the tumor tissue in the "cystic membrane". In the present material, cyst were found in 39 of the tumors—in some cases even multiple cysts. They were all richly vascularized, often showing small hemorrhages, preferably in the necrotic areas, more or less extensive, in all the tumors.

Microscopically the tumors show polypous extensions out into the surrounding brain tissue, most often along the blood vessels. A tumor capsule, in the true sense of the term, could not be demonstrated in any instance, but many tumors were surrounded by glia proliferation. A more frequent finding, however, consisted in edema and beginning necrosis of the infiltrated and surrounding brain tissue. Connective tissue regeneration was seen in a few necrotic areas, but as a rule connective tissue occurred only in the tumor, as a part of the tumor formation itself.

Often proliferation of blood vessels is seen in the surrounding brain tissue—but without such proliferation of adventitia and endothelium in the vessels as is seen in glioblastomas and in the brain tissue surrounding these tumors. The various forms of tumors here observed appear to differ in their tendency to undergo necrosis, but a numerical account of this is not practicable, as in many of the cases a greater part of the tumor was lost through the suction, only a small portion being available for microscopic examination.

If, finally, we are to compare the frequency of the various forms of intracranial metastases occurring in this material and

the number of corresponding primary carcinomas in the material published by the Cancer Register (J. Clemmesen & T. Busk: *The Incidence of Malignant Diseases in Denmark, 1942-1944*. Acta radiol. 24:321-335, 1948), we have among the women carcinoma of the breast in 2313 cases, cancer of the stomach in 1032, carcinoma of the lungs in 121, carcinoma of the uterus in 2174, malignant tumors of the ovary in 524, skin tumors in 782, and carcinoma of the kidney in 136. Among the men, cancer of the stomach occurred in 1618, cancer of the lung in 448, carcinoma of the kidney in 156, and malignant skin tumors in 1010. If all carcinomas showed the same tendency to give intracranial metastases, according to these figures there should be far more metastases in the men from cancer of the stomach than from carcinoma of the lung, and among the women metastases from the uterine tumors should be most frequent. As we have seen, this is far from being the case. But it is a striking phenomenon that the tendency to intracranial metastasis is quite preponderant among supradiaphragmatic tumors. Conceivably this may be associated with the circumstance that the venous blood from these tumors does not enter into the portal circulation but runs directly to the heart or, in cases of pulmonary carcinoma, directly into the arterial blood stream. For in the case of intracranial metastases we may reckon exclusively with metastasis by way of the blood stream, as there are no lymphatics in the central nervous system.

The only subdiaphragmatic tumor showing a tendency to frequent intracranial metastasis is the hypernephroma. In view of its relatively infrequent occurrence, this form of tumor is represented by intracranial metastasis in strikingly many cases in this material, but the venous blood from these tumors also runs directly into the vena cava inferior and does not enter into the portal circulation.

Even though the percental tendency of the individual carcinomas to intracranial metastasis has been calculated—as well as the age distribution of the patients, the duration of illness, and

the period of survival—the number of patients here is too small for a tenable statistic material. It may merely offer some suggestions.

SUMMARY

An account is given of a surgically treated material of 82 cases of intracranial metastasis of carcinoma (32 women and 50 men).

Among the men, the form of carcinoma which most often gives intracranial metastasis is carcinoma of the lungs; in women it is carcinoma of the breast.

The interval between the appearance of symptoms of the primary tumor and those of the intracranial metastasis is investigated. In surprisingly many cases the first clinical symptoms arise from the intracranial tumor. Also the age distribution and the postoperative lifetime are calculated.

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Autopsy Findings in Brains of Mental Defectives

By

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The patients in an institution for mental defectives represent all degrees of defects of intelligence from simple-mindedness to the utmost degrees of idiocy, in which state the patients are merely vegetating beings without any mental life. So, a priori, it would be reasonable to expect that the autopsies on the brains of these patients would give a variegated picture, the causes of mental defects being manifold.

If we are to get beyond the stage at which the institutions for mental defectives are mere asylums, and if we are to hope for some form of therapy or to adopt prophylactic measures with regard to mental defectives, considerable importance will be attributable to the causes of mental defects revealed in this way and to their mutual numerical relations. In this respect the autopsy findings, including microscopical examination of the brain, may offer valuable information. We have therefore gone through the autopsy findings from 46 patients who died at Andersvænge within the period of 1942 to 1949, and we have correlated these findings with the anamnestic data and the clinical features recorded in these cases in order thus to attain a better way of diagnosis and possibly find certain principles applicable to future cases.

Considering first the material from a pathologico-anatomical point of view, it may be divided into congenital anomalies—abnormal *anlage* with resulting abnormal development of the brain—and acquired affections of the brain.

Group I, congenital anomalies, comprises 22 patients:

Group I a: 11 cases with congenital cerebral dysplasia,

" I b: 6 " of mongolism,

" I c: 1 case " phenylpyruvic oligophrenia,

" I d: 1 " " diffuse leukencephalopathy,

" I e: 2 cases " tuberous sclerosis,

" I f: 1 case " callosal agenesis.

Group II, acquired affections of the brain, comprises:

Group II a: 5 cases of infectious or postinfectious lesions,

" II b: 6 " " porencephalia,

" II c: 7 " " atrophy of uncertain origin,

" II d: 3 " " status marmoratus,

" II e: 2 " " senile changes,

" II f: 1 case " kernicterus.

Group I a.

This group of congenital dysplasias is rather heterogeneous. Considering first the weight of the brain, even this will give some valuable information, as microcephalia was found in 4 patients, between 11 and 30 years old, in whom the weight of the brain was under 1000 g., which is the lower limit for a normal adult brain. In these 4 patients the average weight of the brain was 820 g., which represents the normal brain weight in a child of 1 year, while the brain of the new-born normally weighs 370 g.

In a boy of 4 years the weight of the brain was 1475 g., *i.e.* an unquestionable case of megalcephalia. Owing to post-mortem changes in this case, the histological examination offered no additional information. In the 4 microcephalic patients the cortical

stratification was defective or absent, and the nerve cells were fewer than normally as well as defective in their development. Also the myelinization was defective. In contrast hereto, the basal ganglia, the brain stem and the cerebellum appeared normal.

In one patient with normal brain weight the grey substance of both parietal lobes showed pronounced heterotopia. Correspondingly, there was complete disorganization of the grey matter with undifferentiated nerve cells and more glia cells than normally.

Another patient showed microgyria with undeveloped nerve cells, especially in the 3rd and 5th layers, whereas the brain was normal in size. The last 4 patients in this group showed macroscopically normal brains. But histological determination revealed abnormalities in the cortex, with fewer nerve cells than normally, many of which were defective in their development, and some showed lipofuscin deposits, which must be taken as evidence of degeneration.

Group I b.

Among the Mongols the brain weighed about 1100 g. in 4 cases, 620 g. in a child of 2 years, and 700 g. in a child of 11 years. In all 6 brains the cortex showed no stratification, and the nerve cells were poorly developed and scattered diffusely. In those cases where the brain was normal in size there was a considerable accumulation of glia cells, especially beneath the pia. The pituitary was examined in 4 cases, and eosinophilia was found in 3, normal conditions in 1.

Group I c.

The patient with phenylpyruvic oligophrenia was 27 years old, showing megaloccephalia, his brain weighing 1550 g. Histological examination showed normal conditions in the cortex but abnormal nerve cells were scattered diffusely in the basal ganglia.

Group I d.

The patient with leukencephalopathy was 2 years old, showing microcephalia (brain weighing 650 g.). The ventricular system was absent on the right side, with the exception of the right posterior horn. Pronounced gliosis throughout, especially on the right side and proliferation of ependyma in the white substance, with poor myelinization.

Group I e.

In one of the patients with tuberous sclerosis the autopsy showed macroscopically as well as microscopically a typical picture with a large tumor-like formation pressing against the ventricular system, and consisting of polygonal cells, several of which were giant cells. Clinically the other patient presented a typical picture with sebaceous adenoma, epileptic attacks and imbecility, but neither macroscopical nor histological examination of the brain revealed any definite evidence of tuberous sclerosis. Only focal disturbances were seen in the cyto-architectonic structures of the frontal lobes, with subpial glia proliferation; in addition there was depositing of lime concretions in the globus pallidus.

Group I f.

One of the patients with callosal agenesis also showed slight dysplasia of the cortex.

On summarizing, it may be said that the embryonic anomalies chiefly are localized to the cortex. Exceptions to this rule are the patients with phenylpyruvic oligophrenia and with leukencephalopathy.

Turning now to Group II, we meet with a more polymorphous picture.

Group II a.

Among the 5 patients with infectious or postinfectious lesions there are 3 with microcephalia and internal hydrocephalus. In these cases there was atrophy of the nerve cells in the cortex, with surrounding glia proliferation, and also proliferation of the subpial fold of the glia. In one of them also the cerebellum was involved in the atrophy. There was fibrous thickening of the leptomeninges with round-cell infiltration in various degrees; and in 2 cases there was ependymitis granularis. One patient had slight megalcephalia, with the brain weighing 1430 g., and here, besides the above-mentioned changes, histological examination also showed loss and atrophy of the nerve cells in the substantia nigra, indicating a past encephalitis. Finally, the fifth patient showed a typical picture of paralytic dementia, the affection involving especially the third layer of nerve cells in the cortex, and the putamen.

In 4 of these patients the cerebral *anlage* appears to have been normal, and the changes observed in the first 3 brains with hydrocephalus and fibrous leptomeninges are certainly due in part to the inflammation, partly to the secondary fibrosis of the leptomeninges, compromising the circulation of the cerebrospinal fluid. In the patient with dementia paralytica the picture is clear-cut. The fifth patient with megalcephalia probably represents a mixed origin with abnormal factors and exogenous causes: encephalitis.

Group II b.

The 6 porencephalic patients present an even more motley picture than the preceding group. Still, they all have one feature in common: microcephalia, with the brain weighing between 325 and 750 g. Among these patients 4 showed polyporencephalia, in 1 with communication to the dilated ventricular system. The brain tissue surrounding the "cysts" was degenerated, with round-cell infiltration, glia proliferation, a varying number of vessels,

and in some cases an accumulation of blood pigment-containing macrophages. In all the cases the leptomeninges showed fibrous thickening, at any rate in parts, with round-cell infiltration in various degrees. In some of them an affection was found in the cortex, in others in the basal ganglia or preponderantly in the white matter. In some gyri the nerve cells were not yet fully developed, resulting in microgyria.

In these patients undoubtedly the microcephalia does not signify an abnormal cerebral *anlage*. Everything considered, it seems to indicate that here we are dealing with sequelae after hemorrhages or inflammations in early infancy with subsequent defective postnatal growth and development of the brain, perhaps due in part to compromised outflow of the cerebrospinal fluid. The porencephalic cavities result from necrotizing processes in the brain, as the infantile brain is found to be more liable to cystic degeneration than are brains in which the myelinization is completed.

Group II c.

Among these patients 5 presented microcephalia; they were from 14 to 70 years old, with an average brain weight of 900 g. In all of these cases there were fibrosis of the leptomeninges, subpial glia proliferation, and degeneration of the nerve cells in the cortex, together with atrophy of the corona radiata, but only moderately dilated ventricles. Also the basal ganglia showed chronic nerve cell degeneration and, in one case, additional atrophy and neuronophagia of the nerve cells in the pons. No inflammatory changes were seen nor remnants from hemorrhages, and thus the histological findings allow of no inference concerning the etiology of the brain lesion—which, according to the present evidence, seems most likely to be atrophy, not dysplasia.

The sixth patient was a man, 60 years old, with a macroscopically normal brain, weighing 1180 g. But microscopy of the brain showed subpial glia proliferation, degeneration of the nerve cells and neuronophagia in the outer layers of the cortex and the

corpus striatum, which also showed deposits of lipofuscin in the nerve cells.

In all these brains, moreover, there was scattered accumulation of corpora amylacea. In these cases, too, we are unable to say anything about the cause of the lesion.

In the last case, too, the brain appeared in the outside to be macroscopically normal, but the dura was markedly thickened with yellowish patches of exudate on the inside of the dura over both hemispheres, and the leptomeninges were greyish in colour and thickened, too. On section of the brain in the frontal plane an enormous internal hydrocephalus was revealed, with particular preponderance of the anterior horns. The histological examination indicated that here we were dealing with the remnants of a subdural hematoma, the microscopical examination showing vascular and hypertrophic pachymeningeosis. The cortical layers were narrowed down with moderate chronic nerve cell degeneration here and in the nucleus caudatus.

Group II d.

The 3 patients with status marmoratus showed also other changes in the brain, e.g. microcephalia with an average brain weight of 890 g., fibrosis of the leptomeninges with remnants from an old hemorrhage in one case, moderate degeneration of the nerve cells in the cortex, atrophy and abnormal configuration of the basal ganglia with abnormal myelinization and gliosis. This lesion is no longer reckoned as belonging to the group of dysplasias, but to acquired forms of atrophy, probably from anoxia or hemorrhage (which was confirmed by the findings in one of these patients) resulting in irreparable changes localized, above all, to the basal ganglia.

Group II e.

These 2 patients, respectively 54 and 71 years old, presented brains of normal size. The presence of earlier abnormalities is covered up by atherosclerosis, senile changes in the brain with

plentiful depositing of lipofuscin in the nerve cells, atrophy of these cells, glia proliferation, but no definite senile plaques, and by numerous corpora amylacea.

Group II f.

The only patient with kernicterus was 22 years old. His brain was normal in size, but there was pronounced internal hydrocephalus and moderate atrophy of the basal ganglia, where microscopical examination revealed a peculiar yellowish pigment, partly deposited extracellularly, partly absorbed by degenerated nerve cells. Also the cortex showed moderate degeneration of the nerve cells, but no depositing of pigment.

Summarizing these findings, it may be said that the acquired forms of oligophrenia show a more variegated picture than do the dysplasias. Evidence of degeneration is found in all parts of the brain. It is reasonable, therefore, to expect the clinical picture presented by these patients to be more variable than that of the patients with various forms of dysplasia—that is, when we consider the entirely neurological changes.

Turning now to consider the material from a clinical point of view, we find that of the 46 patients 26 were men, 20 women, 13 of them being children, up to 14 years old.

Distributing the patients after their degrees of intelligence, we have: 4 simple-minded, 15 imbecile, and 27 idiots. Table 1 gives a schematic survey of the material, showing that more than one half of the idiots (16 out of 27) have had some exogenous lesion as the cause of their mental defect, whereas the imbeciles are distributed fairly equally between dysplasia and exogenous lesions. The number of simple-minded is too small to allow of any conclusions, but in the present material all 4 patients have had affections of exogenous origin.

The mortality among the simple-minded is low, and their age at the time of their death is high in comparison to the correspond-

ing figures for the higher degrees of mental defects, in which psysical defects also are more frequent for the exogenous forms.

The average age at death was 60 years for the simple-minded, 36 years for the imbeciles, and 16 years for the idiots. The average weight of the brain was 1120 g. in the simple-minded, 1066 g. in the imbeciles, and 890 g. in the idiots. This means, then, that among the idiots the average weight of the brain is the same as that for normal children of one year.

TABLE 1.
Schematic survey of the material.

	Simpleminded	Imbeciles	Idiots	Total
Dysplasia		6	5	11
Mongolism			6	6
Phenylpyruvic oligophrenia		1		1
Leukencephalopathy			1	1
Tuberous sclerosis		1	1	2
Callosal agenesis		1		1
Infectious, postinfectious		1	4	5
Porencephalia		2	4	6
Atrophy of unknown origin	2	1	4	7
Status marmoratus		1	2	3
Senile changes	2			2
Kernicterus		1		1
Total	4	15	27	46

Megalocephalia with a brain weight between 1430 g. and 1550 g. was found in 2 imbeciles and one idiot.

Disposition to mental defects and psychosis is found in 30 per cent of the cases of the total material, but far more frequently in the endogenous group. It is a noteworthy fact that 3 of the 6 mongols have a family history with mental defects among the nearest relatives.

Severe organic defects—e.g. paralysis and epilepsy—are most common in the exogenous forms, especially in porencephalia and the postinfectious forms, among which neurological changes are recorded in every case. The patients in whom also the cerebellum

was involved also showed hypotonia and weakening of reflexes; in the other cases there were spastic conditions with accentuated reflexes, if there were extremital pareses. The endogenous forms, on the other hand, not infrequently present some other congenital organ defect in the form of malformation, and here we also often meet with epilepsy, but only seldom with extremital pareses. Furthermore, the endogenous forms often present some changes also in the endocrine glands, especially in the pituitary (eosinophilia in mongolism), in the genitals, which are atrophical, and in the sinus, which shows a tendency to hyperplasia.

Among the endogenous forms data on abnormalities at birth were recorded only in 3 cases, whereas protracted labour or premature delivery have been recorded in 8 of the exogenous forms. These cases imply a possibility of anoxia with subsequent ischemic changes in the brain or hemorrhages with subsequent degenerative phenomena. (It is to be mentioned that on this point the case records give only defective information). In keeping with this, it may be mentioned that data of this kind were recorded for 4 of the porencephalic patients. In one of these cases the mother had a severe abdominal contusion in the 7th month of pregnancy. Another of these patients had meningitis at the age of 1 month.

Among the 5 patients referred to the postinfectious group, positive data on the infection were available only in the case of a patient who had dementia paralytica, and in whom the presence of syphilis was ascertained at the age of 4 years.

The mother of the patient with kernicterus has subsequently, on request, furnished the information that prior to the birth of this child she had aborted once (in the 4th month of pregnancy) and that she has had no children since. No examination for rhesus factors was made, but these data, together with the really pathognomonic findings, indicate that this was a case of erythroblastosis.

CONCLUSION

The conspicuous pathologico-anatomical changes in the present material emphasize the difference in the brains of mental defectives and insanes, inviting to further studies, and also illustrating the importance of a thorough history of the patients, especially with data on the course of the birth, rhesus factors and infections in early infancy. Finally, attention should also be paid to diseases that the mother possibly may have been suffering from during pregnancy, for perhaps we shall be able to make some advance along this road, too—as is evident from the more recent discovery that deaf-muteism in children may be due to infection of the mother with German measles at a certain juncture of pregnancy.

As to the idiots, in whom the brain has often remained at the infantile stage, one can hardly help thinking that here we are dealing with certain deficiencies that assert themselves and prevent the brain from developing normally. If in the care of mental defectives we are to reach beyond the entirely pedagogic treatment of the patients, just as in the care of epileptics, which now has turned into an active therapy, we shall have to set in with modern methods for neurological examination—*e.g.* pneumography and electroencephalography—and more extensively try to elucidate the physiological conditions with regard to still unknown metabolic anomalies, as phenylpyruvic oligophrenia has opened wide perspectives.

If in future we lay more stress upon these things and continue the microscopical examination of the brains, we shall first be enabled more exactly to classify the various forms of mental deficiencies. When this condition is fulfilled we shall be able to go on with hygienic and eugenic measures—*e.g.* induced abortion in hereditary forms of mental deficiency—and endeavour to avoid birth injuries—perhaps by more intensive employment of caesarean section. Surgical therapy may become topical in some

cases of porencephalia. And it is to be hoped that in future we shall be able to find other rational forms of therapy in this kind of cases.

SUMMARY

A survey is given of the autopsy findings in 46 mental defectives. It is surprising how conspicuous pathologico-anatomical changes may be found in such cases.

The material is divided into the congenital dysplasias and the exogenous forms of mental deficiency.

The pathologico-anatomical findings are correlated with the clinical features.

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Tumors of the Brain Occurring in Childhood¹

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Brain tumors occurring in childhood present a problem which involves not only the neurologic surgeon and the neurologist but every physician who comes in contact with the child. Neurologic surgery has advanced through the co-operation of the general practitioner, the internist, the pediatrician, the neurologist, the ophthalmologist, the pathologist and the radiologist, who contribute to the early diagnosis, for with the improvement in surgical technic has come the realization that early diagnosis is important and early recognition of symptoms is necessary if successful surgical intervention is to be accomplished. The contributions to our knowledge of neurophysiology, as well as general physiology, antibiotics, preoperative and postoperative care during the war have enlarged the sphere of neurosurgery and aided in the diagnosis and treatment of tumors of the brain.

The usual objective signs of intracranial tumors are those of increased intracranial pressure, unsteady gait and visual disturbance. In early childhood increased intracranial pressure may be

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expressed by an increase in the size of the head of the child whose sutures have not become fixed. Thus an enlarging head may be the earliest symptom of an intracranial tumor. There are many more symptoms which it would be well to suspect, such as unsteadiness of gait, dizziness, unilateral deafness, roaring noises in the ear, gradual progressive paralysis, especially of one side of the face or body, unexplained partial loss of vision, causing the child to bump into doors or into other people, and unexplained convulsive disorders. Similar to other clinical entities which have had cardinal symptoms designated as pathognomonic, the presence of the three assigned to brain tumor may indicate that the disease is far advanced and therefore carries a greater mortality rate and a lessened chance of restoration of function.

The differential diagnosis of brain tumors in adults is usually much easier than in children. Children may suffer from nausea and vomiting, which in the early stages of increased intracranial pressure may be confused with acute appendicitis. In view of the fact that nausea and vomiting are also symptoms of other common childhood diseases, an early diagnosis of brain tumor is sometimes confused by an overlay of systemic conditions.

In an attempt to correlate some of the symptoms as well as physical findings with the pathology and the life expectancy of tumors of childhood we reviewed 606 records of children less than 15 years of age, including all those observed from 1907 (the earliest record available) to 1946 inclusive. In this group 427 tumors were verified histologically from tissue removed at operation or at necropsy. The interpretation in all cases has been reviewed and recorded. In 73 cases the presence of a tumor was verified by the surgeon but no tissue was obtained for further study. In 106 cases no tumor was found at operation, or no exploration was undertaken, and we were unable to obtain any information as to subsequent events. These latter two groups of cases have not been included in our series.

In the diagnosis of tumors of the brain, probably the most important examination is a complete and comprehensive neu-

rologic examination, any changes in reflexes, motor and sensory abnormalities, any deviation from the normal in posture, gait, state of equilibrium and mental acuity being noted. Ataxia was noted in 244 of the 427 cases.

The cardinal symptoms already referred to are produced by increased intracranial pressure due either to tumor of the brain or to inflammatory lesions such as arachnoiditis or abscess. Intracranial or extradural hematomas may cause the same type of symptoms.

Headache is the most common of these symptoms, although many brain tumors grow to a considerable size without producing it. As a symptom it was found in 349 of the 427 cases. More than half of the headaches resulting from increased intracranial pressure are not localized to a definite region or even to one side of the head but are diffuse. Generalized headaches caused by intracranial pressure are usually deep and expanding; seldom are they continuous; they occur intermittently, usually in the morning or every two or three days, and may be relieved by vomiting.

Vomiting associated with brain tumor may or may not be associated with headache. If it is associated with headache, it is followed by relief of the headache. It may or may not be associated with nausea, but it is not related to eating of food. Explosive or projectile vomiting, while not essential, is suggestive of intracranial pressure. The relief of headache by vomiting is much more suggestive of brain tumor than the character of the vomiting. Vomiting occurred as a symptom in 341 of our 427 cases.

The third cardinal symptom has to do with the eyes and may be indicated by loss of visual acuity. It is this symptom that the ophthalmologist has interpreted in terms of intracranial pressure and thus has aided in the early diagnosis. An examination of the eye grounds is necessary to determine the presence of papilledema or choked disk. Papilledema or choked disk was found in 311 of our 427 cases. Examination of the fundi with the

ophthalmoscope is important in determining the presence or absence of hemangiomas of the fundi. This finding is almost pathognomonic of hemangiomas of the brain, usually in the cerebellum.

Convulsions may indicate increased intracranial pressure or localization of the lesion. Tonic convulsions seem to arise from a lower level in the brain than that from which the clonic type arises. Whenever the convulsions involve one side of the face, or one arm or leg, they are of localizing value and indicate a lesion involving the contralateral motor area.

The roentgenographic examination of the head is important with regard to calcification within the lesion or about the sella turcica, localized changes in the bone, enlargement of the sella turcica, air in or about the lesion, and increased vascularity of the bone.

Calcification within the lesion itself is present in only a small percentage of abnormal conditions. Such structures as the pineal gland, the pacchionian bodies and the choroid plexus may normally in the adult exhibit a certain amount of calcification. Areas in the falx or the tentorium frequently described as calcification should probably more properly be considered as ossification. Lesions that may exhibit regions of calcification include tumors, hematomas, tubercles, cysts, old abscesses, regions of old meningeal lesions, encephalitis and aneurysms. Calcification occurs in about 12 per cent of the gliomas and in 70 per cent of suprasellar cysts, which are usually tumors of Rathke's pouch.

In a series of 384 of our cases in which roentgenograms were studied, the findings indicated the presence of tumor in 267 (69.5 per cent). The following findings were suggestive of, or indicative of, intracranial tumor: (a) separation of sutures; (b) erosion of the clinoid processes; (c) erosion of the floor of the sella; (d) abnormal areas of calcification; (e) erosion of, or lateral thinning of, areas of the frontal, occipital or parietal bones.

With the development of neurologic surgery as a specialty it has become more apparent that a great number of tumors of the

brain which are diagnosed early in their development are amenable to surgical treatment. This applies not only to the benign, encapsulated tumors but also to the infiltrating gliomas. However, in the early stages of development of tumors of the brain the symptoms are sometimes so vague and uncertain that a definite diagnosis is impossible. In this event one of two courses is open from the diagnostic standpoint. Sometimes it is necessary that a patient be kept under observation until more definite evidence becomes apparent or encephalography or ventriculography can be carried out. Probably the greatest contribution to the early diagnosis of brain tumors is the injection of air within the intracranial cavity by the lumbar or the ventricular route. These procedures should be carried out only after a very careful general, ophthalmologic, roentgenologic and neurologic examination and should never be considered without a full realization of the risk incurred.

Encephalography, or the removal of cerebrospinal fluid and injection of air through the lumbar route, should never be undertaken in the presence of increased intracranial pressure as evidenced by choked disks or papilledema. Much emphasis has been laid on the danger of performing lumbar punctures in the presence of increased intracranial pressure, and it is even more hazardous to attempt the removal of fluid from the subarachnoid space and its replacement with air. In the presence of increased intracranial pressure, ventriculography, or the removal of cerebrospinal fluid and replacement by air from the lateral ventricles, is the operation of choice. It, also, carries a certain hazard, but this is minimized when craniotomy is performed immediately afterward. Roentgenograms taken after the injection of air through either the lumbar or the ventricular route furnish a great deal of information with regard to intracranial contents. A normal distribution of air in the subarachnoid space, in and around the convolutions of the cortex and within the ventricles rules out the possibility of an intracranial lesion.

One of the advancements in the diagnosis of intracranial lesions has been the so-called electro-encephalogram. Electro-encephalography, a technic whereby the electrical activity of the human cerebral cortex is recorded either through the intact scalp or with electrodes in contact with the cortex, has become almost a routine procedure in many clinics. When electro-encephalography was first introduced, there were hopes that this procedure would develop into a diagnostic tool of wide applicability and that it would provide a fruitful approach to an understanding of human behavior. Like other laboratory technics, however, electro-encephalography can never replace careful clinical observation, neurologic examination and mature clinical judgment.

The electro-encephalographic records obtained through electrodes applied to the scalp record minute electrical potentials arising from the cortical tissue close to the electrode. Normal electro-encephalograms range from very rhythmical, regular, well-synchronized records with frequencies from 8 to 12 per second to irregular, poorly synchronized records in which frequencies are poorly defined. However, it has been found that under comparable conditions the electro-encephalogram on the same person remains remarkably constant from day to day and even from year to year. There is an over-all characterization which cannot be adequately defined in terms of any such property as frequency or amplitude, which has been compared by some to the constancy of facial features and which may be almost of identifying value for individuals.

Not only in the localization of tumors of the brain has electro-encephalography been investigated as a diagnostic aid but also as an indicator as to the pathologic character of the tumor. Williams and Gibbs (1) stated that by correlating the frequency and amplitude of pathologic waves with position and extent of the discharge it was sometimes possible to surmise the nature of the lesion. Greenstein and Strauss (2) reported 47 cases of glioma and 8 cases of metastatic carcinoma. In 74 per cent of the spon-

gioblastic tumors the focal per cent time delta was 40 or more. In 10 per cent of the transitional and in none of the well-differentiated gliomas was it 40 or more. These results seem to indicate that a focal per cent time delta of 40 or more is strongly indicative of spongioblastic or metastatic carcinomatous tumors. Reese and Masten (3) further expressed the belief that there is a definite correlation between the rapidity of growth and the percentage time wave deltas of the abnormal electro-encephalogram.

According to Drumheller, Keith and Bickford (4) a study was made of the electro-encephalograms of 50 children seen at the Mayo Clinic with proved neoplasms of the brain. In 9 (75 per cent) of the 12 children who had tumors of the cerebral cortex their localization as indicated by the electro-encephalogram was correct. In 8 children with supratentorial tumors over or near the brain stem no localizing or consistent electro-encephalographic pattern was obtained. In 21 (70 per cent) of 30 children who had tumors of the posterior fossa a bilateral abnormality was observed in the electro-encephalograms recorded from the occipital region or occipital and contiguous regions. It is acknowledged that the abnormality found in this last group is also found occasionally in normal children, as well as in cases of epilepsy, occipital lobe tumors or allergic disorders. These conditions usually can be excluded on the basis of the history and by use of other laboratory aids. Electro-encephalography in the study of brain tumors in children should be considered, not as an infallible test but rather as a diagnostic aid to be used with the help of the history and other diagnostic aids.

In emphasizing the importance of early diagnosis of brain tumor from the standpoint of earlier operation, another development in the diagnosis of intracranial lesions, cerebral angiography, has enabled us to differentiate between vascular lesions and neoplastic lesions. A radiopaque substance is injected into the carotid or vertebral arteries, and subsequent roentgenograms are made of the head. In this way the vessels are outlined.

Ingraham and Cobb (5) reported on 25 patients ranging in age from 1 year and 10 months to 68 years who received two or more injections of 10 cc. of 35 per cent iodopyracet (diodrast) during the ensuing three years. Iodopyracet is a suitable medium for cerebral angiography. It is inert in the body, quickly excreted and highly soluble. If large quantities of a concentrated solution are used in angiography, reactions attributable to hypertonicity of the solution may be encountered. To obviate occurrence of reaction, a method of injecting small quantities of dilute solution of iodopyracet with a special angiogram needle was presented. Iodopyracet appears to be a safe contrast medium for cerebral angiography for both adults and children when used in the way described by Ingraham and Cobb (5). Roentgenograms of satisfactory quality are secured and several injections may be made for stereoscopic arteriograms, for anteroposterior projections and for demonstration of two or more of the four arterial networks of the brain.

While it is universally recognized that early diagnosis and early operation are of extreme importance, there is little evidence brought out by history or examination to help determine the pathologic nature of the intracranial lesion. It is only at operation with removal of tissue for microscopic diagnosis that a definite diagnosis can be made. It was thought at one time that a short history with rapid progression indicated a highly malignant and inoperable lesion. However, time and again we have seen patients who give a short history with rapid progression but who are suffering from benign, operable and removable lesions. For that reason it is the consensus that every intracranial lesion should be operated on as early as the diagnosis can be made and localization can be ascertained. Only in this way can one determine the possibility of operation on the lesion, and when the malignant type of the glioblastic tumors is encountered, it is also the consensus that as radical a removal as possible should be attempted.

TABLE 1.
427 Verified Tumors¹.

Tumors	Total		Age of patients			
			Birth-5 year		6-14 year	
	Patients	Per cent	Patients	Per cent	Patients	Per cent
Total	427		108		319	
Astrocytoma	104	24	29	27	75	24
Medulloblastoma	86	20	26	24	60	19
Ependymoma	49	11	18	17	31	10
Glioblastoma multiforme	40	9	5	5	35	11
Craniopharyngioma	23	5	5	5	18	6
Sarcoma	16	4	6	6	10	3
Ependymoblastoma	14	3	3	3	11	3
Astroblastoma	14	3	1	1	13	4
Pituitary adenoma	10	2	0		10	3
Meningioma	11	2	3	3	8	2
Pinealoma	10	2	2	2	8	2

¹ Gliomas 359 or 84 per cent.

The following tumors appeared in very small numbers: glioma (unclassified); oligodendroblastoma; glioma from granular layer of cerebellum; polar spongioblastoma; epidermoid; hemangioma; malignant neoplasm; xanthoma; cysts and gliosis; cholesterolithoma and chordoma.

In our series of about 600 tumors occurring in children who have been examined at the clinic, 427 of these (table 1) were confirmed by the pathologist on the basis of study of tissue removed at operation. Surprisingly enough it was found that instead of the malignant medulloblastoma the more benign astrocytoma and ependymoma predominated. The cases were divided according to the type of tumor present and the length of survival of the patient after operation. Although the immediate mortality rate was rather high in the early days of the series, with the advancement of knowledge of the symptoms of tumors of the brain in children and improvement in surgical technics, patients were sent to the neurologic surgeon earlier in the development of the disease. It was apparent that the early diagnosis of tumors

of the brain in children allowed earlier operation, and as the years progressed, not only was the mortality rate lowered but the number of one-year to five-year survivals was greater. Thus the conclusion drawn from this study was that the early diagnosis of tumors of the brain in children is associated with a greater percentage of operability, lessened morbidity and mortality rates and a greater life expectancy.

Of the 427 confirmed tumors mentioned in the preceding paragraph 359 were gliomas (84 per cent). Cushing (6) found that 42.6 per cent of all brain tumors were gliomas. Elvidge, Penfield and Cone (7) found that 44.9 per cent of their series of 467 verified tumors of the brain and cord were gliomas. Baker (8) gave 61.8 per cent of his series as gliomas, and Bennett (9) reported 62.9 per cent of the primary intracranial neoplasms observed at the Army Institute of Pathology as gliomas. This last group included only persons from 18 to 38 years of age. Smith and Fincher (10) in 1942 reported that 86 per cent of 87 verified tumors in children were gliomas. This corresponds closely to our figure of 84 per cent.

Astrocytoma was the most frequent tumor, being present in 24.4 per cent of the cases. Medulloblastoma was a close second, being present in 20.1 per cent. Ependymoma was present in 11.4 per cent; glioblastoma multiforme in 9.3 per cent; craniopharyngioma in 5.4 per cent. All other tumors together constituted 29.4 per cent.

It was of interest to us to determine whether the incidence of certain tumors was greater or less during the first five years of life than among older children. Astrocytomas occurred in about the same number in both the group from birth through 5 years (26.9 per cent) and the group from 6 through 14 years (23.5 per cent). Medulloblastoma was somewhat more common in the younger group (24.1 per cent) than in the older (18.8 per cent). Ependymomas were also somewhat more common in the younger group (16.6 per cent and 10 per cent). Glioblastomas were considerably less common in the younger group (4.6 per cent

and 10.9 per cent). The more rare types of tumor were rather more common in the older than in the younger group.

It is well recognized that infratentorial tumors are more common in children than supratentorial. In our series 65.8 per cent were infratentorial and 34.2 per cent were supratentorial. This is in almost exact agreement with Cushing's figures (65 per cent). In the children through 5 years of age, 71.3 per cent were infratentorial and 28.7 per cent were supratentorial, but in the older group 63.9 per cent were below the tentorium.

Two hundred and eighty-one tumors were infratentorial. Eighty-five (30.3 per cent) were astrocytomas and 84 (29.9 per cent) were medulloblastomas. There were 35 ependymomas (12.5 per cent) and 19 glioblastoma multiforme (6.7 per cent). There were 58 other tumors of less common types (20.6 per cent).

One hundred and forty-six tumors were situated above the tentorium. There were 23 craniopharyngiomas (15.8 per cent), 18 astrocytomas and 18 glioblastoma multiforme (each 12.3 per cent), 13 ependymomas (8.9 per cent); 10 pituitary adenomas (6.9 per cent) and 64 other tumors (43.8 per cent).

The location of the brain tumor, whether deep or superficial, influences the surgical removal and the seriousness of the operation. Frequently this factor alone prevents adequate surgical treatment. In addition, as is well known, many tumors are not encapsulated but infiltrate the soft tissue of the central nervous system readily and widely. These factors naturally affect the prognosis. In an attempt to obtain an over-all picture we divided our series into five-year groups (as to date of operation) and found that under present-day conditions more than 50 per cent of the patients who are traced are alive six months after operation. In the period 1920 through 1924 only 23.8 per cent lived six months or more; 1925 through 1929, 23.3 per cent; 1930 through 1934, 34.3 per cent; 1935 through 1939, 51.7 per cent; 1940 through 1944, 54.3 per cent. Of 347 traced patients 41.2 per cent lived for six months or more; of 327 traced patients 32.7 per cent lived one year or more; of 256 traced patients 13.3 per cent lived five years

or more. The inquiry for follow-up information was as of January 1, 1947.

In a study made with regard to relative malignancy and in an attempt to simplify the terminology of tumors of the brain, Svien and his associates (11) reviewed all the cases from birth until 16 years of age and found that in 130 of them the tumors were medulloblastomas. Of the 130 patients up to 16 years of age there were 96 showing a predominance of medulloblastomas in the earlier years. The average postoperative survival period was 15.4 months. Of the entire group of cerebellar astrocytomas there were 131, 33 occurring in the 0 to 16 year group. Of these 33, 18 (54.5 per cent) were grade 1 and showed an average postoperative survival period of 87.4 months. Breaking these figures down still further, they found that there were 96 medulloblastomas, 94 cerebellar astrocytomas, and 33 ependymomas of the fourth ventricle. In the ratio of malignant to relatively benign gliomas in the cerebellum there were 96 medulloblastomas, 82 grade 1 astrocytomas and 18 ependymomas, or a ratio of 96:100. They concluded that thus when confronted with a child in age group 0 to 16 years with a glioma in the region of the fourth ventricle, there is a 51 per cent chance of finding a glioma in which the postoperative survival period can be expected to be 80 months or more. Moreover, if all of the astrocytomas and ependymomas occurring in this age group are included regardless of the grade of malignancy, there is a 57 per cent chance that one will encounter at operation a glioma and that the postoperative survival period will still be two to three times as long as the 15.4 months one would expect in the case of a medulloblastoma.

Not only has the development of neurosurgery been associated with improved diagnostic methods but certain improvements in technic have developed which have contributed greatly to the lowering of the mortality rate and the securing of permanent cures in the treatment of tumors of the brain. Two complications in the operative recovery after total or subtotal removal of tumor

of the brain have been hemorrhage and cerebral edema. One of the outstanding recent contributions to the technic of neurosurgery has been the development of newer methods of hemostasis. Autogenous muscle pledgets have been used for years for the control of surface bleeding. Thrombin, when applied topically, was found to have the same effect, but when sprayed on the surface of the brain or bleeding dura, it tended to be washed away by the seeping blood. Therefore, substances were sought to use as absorbable sponge material which could be saturated with thrombin. Three such substances were developed. A partially oxidized cellulose, which was prepared in the forms of gauze, cotton and paper, was produced. Although not the best carrier for thrombin, these substances were found to have valuable hemostatic properties of themselves and have been extremely useful, particularly when a small, tight pack was needed for the control of hemorrhage. Both experimental and clinical evidence points to the ready absorbability of this oxidized cellulose when used within the cranial cavity. A new processed oxidized cotton has been developed which may prove to be a more nearly ideal hemostatic agent.

Fibrin foam, a by-product in the manufacture of plasma, can be dried and proved to be a friable, porous material which absorbs thrombin, allowing it to be applied topically in the form of small pledgets. With the cessation of war and the decrease in the manufacture of plasma, fibrin foam became difficult to obtain. For that reason other substances were sought, and gelatin was used to make a foamlike sponge which has proved of great value.

Cerebral edema, associated with the removal of intracranial tumors or posttraumatic lesions, has been a complication which has increased the mortality and the morbidity rates and has been a distressing factor in the convalescence of the patient. Hypertonic solutions have been used; dehydration has been used, but in almost every case there has been some reaction. One of the by-products of plasma fractionation was serum

globulin, and it was found that in addition to being an adequate substitute for the use of plasma in shock, it also proved to be great benefit in cerebral edema as a dehydrating mechanism. At the present time serum globulin as a dehydrating mechanism after head injury or the removal of cerebral tumors is being used and tested. The evidence which we have indicates that this substance would bear further investigation because it can be used in from 50 to 80 cc. with remarkable results as evidenced in the operating room as well as during the postoperative course.

Anesthesia in the operations for the removal of brain tumors has followed a trend away from local or regional anesthesia. The development of different methods of anesthesia, as well as new anesthetic agents, has accounted for this. When local or regional anesthesia was used, the patients complained because of the emotional strain if not the actual discomfort during the operation. It was assumed that general anesthetic agents or the inhalation of ether, chloroform, nitrous oxide and ethylene and the various other agents carried a higher mortality rate, and this was true under previous conditions. However, the introduction of the intratracheal tube allowed for a freer use of the inhalation anesthetic agents with a greater safety from the standpoint of both mortality and morbidity rates. Rectal anesthesia was accepted as a safer method of administering anesthetic agents and is now used in some clinics almost entirely. Intravenous anesthesia has been adopted as a safe method, especially the use of pentothal sodium, which is a rapid anesthetic agent and from which the patient rapidly recovers after cessation of administration of the drug.

The availability of immediate diagnosis through fresh tissue examination in the Division of Surgical Pathology has greatly improved the scope of neurologic surgery. This is particularly true in tumors of childhood because an immediate differential diagnosis can be made between a very malignant tumor and a more benign one. A diagnosis of malignant medulloblastoma once having been made, it is sometimes advisable to limit the

scope of the operation because palliation can be accomplished through roentgen irradiation. If the more benign astrocytoma or oligodendroglioma is diagnosed, then the operative procedure may be more radical. An immediate pathologic diagnosis is of great help to the neurosurgeon if available during the operation.

SUMMARY

Brain tumors in childhood are similar to brain tumors in adults in that early diagnosis allows for early treatment. The history of headache, vomiting, disturbance of vision or clumsy or staggering gait should arouse a suspicion of an intracranial lesion.

The prevalence of the very malignant medulloblastoma has been found to be much less than hitherto suspected. Statistics have shown that the relative frequency of benign and malignant lesions of the brain in children is more encouraging than previously considered.

The success of neurosurgery in dealing with brain tumors in childhood is dependent on the co-operation of the family physician, the pediatrician and others who attend these patients professionally.

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Results of Some Diagnostic Tests in Different Forms of Headache

By

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Headache appears as a symptom in so widely different diseases that its physiological basis appears most likely to be variegated. Therefore, quite naturally, the question arises whether it may be possible to group the clinical types of headache after the physiological mechanism bringing about the headache in the individual cases. The solution of this question has already advanced so far that it seems justified, for instance, to assume that such types of headache as migraine, allergic headache, and histamine hemicrania belong to a group in which the headache is directly connected with dilatation of the cranial blood vessels, a vasodilator group, whereas other types of headache such as myalgic and certain neurasthenic forms hardly may be explained in the same way and thus may not be referred to the same group. Naturally, a grouping along the lines mentioned is not only of theoretical interest, but also of practical-clinical interest, because it may give certain indications for a rational therapy.

The clinical diagnosis is based on various ways of recognition:

(1) The information given by the patient about the character, localization and appearance of the headache will often be of decisive significance to the appraisal of the given case and to the possibility of its grouping within established categories. It is to be emphasized explicitly, however, that it often requires very

persistent, patient, and thorough questioning to arrive at a serviceable result, and it must be kept in mind that the ability of the patient to find adequate terms for his own sensations often is surprisingly deficient.

(2) The objective secondary symptoms accompanying certain types of headache such as migraine and histamine hemicrania are valuable differential-diagnostic points, even though sometimes they may be directly misleading—as in symptomatic migraine.

(3) Attempts at a reconstruction of the constellation of factors that elicit the patient's headache are useful, though rarely practicable. In certain forms of allergic headache and allergic migraine, however, it is possible to perform such a positive test by administration of the allergen in question, thus verifying the diagnosis.

(4) A sort of negative test may be performed, among others, in allergic cases by means of elimination therapy, where absence of headache when the patient is deprived of the actual factor will help to verify the diagnosis.

(5) The favourable effect of ergotamine in migraine cannot be taken as a surely positive test for migraine. For one thing, there are a few cases of migraine which seem rather refractory to ergotamine; and, furthermore, a favourable effect of this remedy is seen also in other types of headache such as, for instance, histamine hemicrania. But, presumably, it is safe to take a favourable therapeutic result as signifying that in the given case the headache belongs physiologically to the same group as migraine.

(6) Something similar applies to antihistaminica. A good effect from such remedies may be seen in allergic types of headache, but these results are not serviceable as a positive test for allergic headache, because the effect is far from being constant, and a favourable effect is seen also in other forms of headache, including histamine hemicrania.

(7) The histamine test. In patients with or without habitual headache, the injection of a suitable dose of histamine, varying

according to the sensitivity to histamine and headache preparedness of the individual, will produce a headache associated with dilatation of the cranial vessels, *i.e.* a vasodilator headache. In allergic conditions histamine and histamine-like substances play a rôle in the development of the allergic manifestations, forming the basis of the vasodilator allergic headache. In allergic migraine the allergen elicits the migraine preparedness of the patient, *i.e.* both the primary vasoconstrictor phase and the secondary vasodilator phase = the headache phase; and it seems obvious that the latter phase is associated with a histamine effect on the blood vessels. In the numerous cases of migraine not recognized as allergic the rôle of histamine as a headache factor is more hypothetical. By means of histamine tests we have tried to ascertain how often a provoked histamine headache was perceived by the patient as being identical with the habitual headache. In the particular form of headache, histamine hemicrania—as we have designated it for differentiation from ordinary histamine headache—two characteristic conditions assert themselves: (1) considerable hypersensitiveness to histamine, so that the attacks are provoked by minimal doses of histamine; and (2) the fact that histamine not only produces the simple vasodilator phase of the headache, just as in all other cases, but the whole attack with redness, edema, rhinorrhea, and epiphora. One feels tempted to assume that histamine in this type of headache plays a similar rôle as the allergen in allergic migraine, because it elicits not merely a vasodilator headache, but a typical polysymptomatic preparedness (migraine or histamine hemicrania).

About the histamine test employed in the present material the following may be mentioned:

After a number of experiments we have arrived at the employment of a relatively weak solution of histamine chloride, $\frac{1}{4}$ per thousand, for tests as well as therapeutically. Our usual test dose is $\frac{1}{4}$ mg. histamine chloride injected subcutaneously. Employment of larger doses too often gave a massive, non-graduated histamine headache in which it was difficult for the patient to

decide whether it had the character of a reproduction of the habitual headache. Employment of weaker doses too often failed to elicit any headache. In a material published before (1), the dose of $\frac{1}{4}$ mg. elicited headache in 75 % of patients with various types of migraine; and 66 % recognized this headache as a reproduction of their habitual headache. The possibility was considered that these histamine-positive cases of migraine perhaps might be particularly amenable to treatment with histamine or anti-histaminica, but our results furnished no decisive evidence to this effect.

Our previously reported cases of histamine hemicrania (2, 3, 4, 5) reacted to minimal doses of $< \frac{1}{10}$ mg. with reproduction of the attacks, and it was not possible in other patients to elicit headache with such small doses.

(8) The nitroglycerin test. Nitroglycerin produces a dilatation of arterioles and capillaries that is of peripheral character, and which is followed by a fall in blood pressure, eliciting via the vasopressor centres a vagus reflex in the form of tachycardia. The dilatation of the cranial vessels gives rise to headache. Nitroglycerin is employed in a headache test by Schnitker & Schnitker (6), who place a tablet of 1.3 mg. sublingually. After 5-10 min. a headache appears that lasts 5-10 min. and may be interrupted by compression of the carotid artery or by intravenous injection of gynergen. The test may be accompanied by general malaise and syncope.

In order to reduce the universal reactions as far as possible and obtain a longer-lasting headache, which, in those cases where the patient is unable to estimate the brief headaches caused by the sublingual tests, should make it possible to estimate the headache more definitely, I have tried to work out a percutaneous test after the following principles:

A 2 % nitroglycerin ointment (Niglin ASA) is used. By means of a spatula it is applied to the frontotemporal region, as a streak of about 1.5 cm. = 6 mg., which is a suitable amount. A number of experiments have established that this form of application

gives hardly any universal by-effects, and still it has a strong cranio-vascular effect. Furthermore, experiments have shown that the localization of the nitroglycerin headache is independent of the question whether the ointment is applied unilaterally or bilaterally.

Shortly after the application a burning sensation of the skin appears beneath the ointment, and within 15 min. the headache makes its appearance, whereas the universal effects are but slightly pronounced. A delayed or weak reaction is often due to the skin and subcutis at the site of application being coarse and infiltrated.

So far, the percutaneous nitroglycerin test has come up to expectations: there has practically been no universal reactions to speak of, and in those cases where the patient has been unable to estimate the quality of the headache at its initial stage, the tardive headache has nearly always made this practicable. Furthermore, when it is desirable to interrupt the headache, this has been possible by removal of the ointment and by intravenous injection of dihydroergotamine, 1 cc. ($\frac{1}{2}$ cc. is insufficient).

We have used the nitroglycerin test (and the histamine test) in the way that we made the patient compare the provoked nitroglycerin headache (or histamine headache) with his habitual headache, and thus decide whether the test headache represented a reproduction of the habitual headache with regard to quality and localization. When this proved to be the case we have concluded that the habitual headache then must be of vasodilator character.

Certain elementary difficulties are connected with the patient's explanations: Often the attacks of the habitual headache are introduced by an aura, which forms a sort of background for the following phase of pain, whereas the test headache exclusively comprises the pain component of the attack, thus appearing without any preparedness. Furthermore, according to our experience, the vocabulary of the patients is strikingly defective

and often misleading with regard to adequate designations; and it has to be kept in mind that a test headache on repetition of the test may very well change in localization and in quality. The results of our tests must be appraised with this reservation and in keeping with the fundamental view that in the individual cases we have tried to reveal the more essential aspects, and that the designation "reproduction of habitual headache" covers all degrees of identity from "reminding of" to absolute identity.

In a preliminary report (7) an account was given of our first test results. Later the material has been supplemented, and now it comprises about 300 nitroglycerin tests, 171 of which cases have been settled. Of this total, 72 patients were also subjected to the histamine test. In this material the distribution of the patients was as follows:

(1) Patients without headache, 19 cases, who practically always had been free from headache and who were not suffering from any organic nervous or mental lesion.

(2) Migraine, 64 cases, typical hereditary forms without particular features.

(3) Vasomotor cephalalgia (*Cephalea vasomotoria*), 12 cases, comprising the often somewhat sympathicotonic forms encountered in the climacterium or at puberty, and somewhat related to the syndrome of migraine rouge.

(4) Neurasthenic headache, 18 cases. The patients in this group are picked out among neurasthenics, the main stress being laid upon the symptoms asthenia and headache, while sympathicotonic, hyperthyreotic and other more complicated forms are excluded.

(5) Psychogenic headache, 10 cases, consisting of patients in whom the headache was referable exclusively to a psychogenic reaction of a depressive character.

(6) Myogenic headache, 19 cases, in which the headache could be explained by the presence of pathological changes in the muscles of the head and neck—confirmed by a physiurgic specialist.

TABLE 1.
Schematic Survey of the Headache Material and its Reaction to the
Nitroglycerin and the Histamine Tests.

	Patients without headache	Migraine	Vasomotor headache	Neurasthenic headache	Psychogenic headache	Myogenic headache
Headache preparedness ...	Nitroglyc. test 53 % Histamine test 42 %	95 % 75 %	100 % 100 %	67 % 23 %	90 % 66 %	68 % 50 %
Reproduction of quality of headache	Nitroglycerin test .. Histamine test	95 % 50 %	100 % 80 %	0 % 9 %	0 % 0 %	0 % 33 %
Reproduction of localization of headache	Nitroglycerin test .. Histamine test	77 % 46 %	92 % 60 %	0 % 9 %	0 % 0 %	0 % 33 %

In addition there are patients with concussion of the brain (5 cases), arterial hypertension (3 cases), intracranial tumor (3 cases), allergic headache (3 cases), cephalalgia of an obscure nature (5 cases), lumbar puncture (2 cases), postepileptic headache (2 cases), sunstroke, menstruation, herpes zoster, edema of the brain, traumatic migraine, and trigeminal neuralgia (1 case of each). All the cases in this heterogeneous group are omitted from the following account.

An attempt has been made on the basis of this material to judge of the quality and localization of the nitroglycerin and histamine test headaches, besides the headache preparedness of the individual groups and the possibility of reproduction of the habitual headache with regard to its quality and localization, together with the effect of the test on an already existing headache (preprobatory headache).

With reference to the difficulties of the appraisal already mentioned above, the results obtained are as follows:

(1) Quality of the test headache: under the percutaneous nitroglycerin tests the quality of the headache was given as thumping (knocking, throbbing) in 77 %, oppressive (pressing, tense) in 14 %, and undefinable in 9 %, whereas the corresponding figures for the histamine tests were 56 %, 36 %, and 8 %, respectively. While thus the undefinable group is the same for the two tests, the nitroglycerin headache is thumping far more often than oppressive, and the histamine test is oppressive almost as often as it is thumping.

(2) Localization of the test headache: at the percutaneous nitroglycerin test the localization of the headache was stated to be frontal in 39 %, occipital in 23 %, fronto-occipital in 24 %, and diffuse in 14 %; with the histamine test the corresponding figures were 33 %, 18 %, 24 %, and 24 %, respectively. From these figures it seems safe to say that there is no difference between the two tests with regard to the localization of the test headache.

(3) Preparedness for headache: from Table 1 it will be noticed that among patients without headache the nitroglycerin test gave preparedness for headache (with regard to vasodilator headache) in a little over 50 %, while the histamine test had this effect in a little under 50 %. It will further be noticed that this difference between the two tests is found also in the special groups. Further, the neurasthenic and myogenic headache groups show only a little more frequent preparedness for vasodilator headache than does the group without headache. But, in particular the neurasthenic group shows much greater preparedness for nitroglycerin headache than for histamine headache, and something similar applies also to the group of psychogenic headache, which also is characterized by increased preparedness for vasodilator headache. The groups of migraine and vasomotor headache show a preparedness for headache amounting to about 100 %—as indeed was to be expected in such forms of vasodilator headache.

It must be emphasized that the generally lower preparedness for headache induced by the histamine test need not be due to any fundamental difference between the two tests, and that it also may be interpreted as a quantitative difference that possibly may be balanced by increasing the histamine dose.

(4) Reproduction of the quality of the habitual headache: it will be noticed that both migraine and vasomotor headache show a practically 100 % reproducibility, corresponding to the preparedness of these groups in the nitroglycerin tests, whereas reproduction of the headache is not nearly as frequent in the histamine test. The neurasthenic, psychogenic, and myogenic headache groups are lacking reproduction of the quality of the headache, which signifies that these forms are not of vasodilator character. In particular it is worth noting that the psychogenic group shows a pronounced preparedness for vasodilator headache. The myogenic group differs from the two other groups by showing reproducibility of the quality of the headache in the histamine test—but the figures for this group are very small.

(5) Reproduction of the habitual localization of the headache: largely this feature follows the reproduction of the quality of the headache, only with a little less frequency. Here, too, the figures for the nitroglycerin test are higher than those for the histamine test.

(6) As to the effect of the test on preprobatory headache it may be said that as far as possible we have avoided applying the tests to patients during attacks of their headache. Still, 7 patients had a relatively mild attack of migraine at the time of the test, and they all reacted to the nitroglycerin test with aggravated headache, identical with the preexisting one. The histamine test was applied to 3 of these patients, in two of whom the headache was aggravated, while it disappeared in the third.

(7) In a number of the above-mentioned cases, electro-encephalography was performed before, during, and after the nitroglycerin and histamine tests—in order to ascertain whether a dysrhythmia would appear as has been observed during the aura of the habitual migraine attack. We found no dysrhythmia, and thus the clinical absence of an aura at the production of the test headache corresponds very well to the electro-encephalographic findings.

SUMMARY and CONCLUSION

After a brief mention of the different criteria for the differential-diagnostic appraisal of the syndrome headache, an account is given of a histamine test with subcutaneous injection of $\frac{1}{4}$ mg. histamine chloride and a new nitroglycerin test with percutaneous application of 6 mg. nitroglycerin by means a 2 % ointment, both of which induce a vasodilator headache. We have found $\frac{1}{4}$ mg. histamine to be most suitable for the purpose of eliciting a vasodilator headache sufficiently often and yet avoid such strong reactions that it may be difficult to appraise the character of the headache. The special nitroglycerin test is introduced for the purpose of eliciting headache with the least

universal reaction possible and at the same time make the headache protracted in cases where the patient has been unable to estimate the character of a brief headache.

In a material of 171 cases, comprising chiefly a group without headache, together with groups of migraine, vasomotor headache, neurasthenic headache, psychogenic headache, and myogenic headache the following features were found: (1) Nitroglycerin headache was thumping more often than was histamine headache. (2) There was no definite difference in the localization of the two test headaches. (3) Preparedness as to vasodilator headache was more pronounced in the nitroglycerin test. (4) There was about 50 % preparedness in the group without headache; and it was just as frequent in the neurasthenic and myogenic groups, and even more frequent in the psychogenic group, and most frequent in the two vasodilator groups—migraine and vasomotor headache. (5) Migraine and vasomotor headache are almost 100 % reproducible as to quality and a little less frequent as to localization, considerably less frequent in the histamine test. The other groups are not reproducible, which is particularly remarkable in the group of psychogenic headache, in which there was a pronounced preparedness for vasodilator headache. (6) Electroencephalography before, during, and after the two tests showed no dysrhythmia. (7) Both tests are considered serviceable (a) for diagnosis of vasodilator headache preparedness, and (b) to ascertain a habitual headache as being of a vasodilator character by means of reproduction. (8) The histamine test is suitable for identification of histamine hemicrania. (9) The cases which in this material have been reproducible by means of the histamine test have not proved particularly amenable to treatment with histamine or antihistaminica. (10) in some of the groups of this material the cases have been so few that the obtained results are to be accepted only with some degree of reservation.

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Ferrous Carbonate in the Treatment of Tic Douloureux

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In 1942 a preliminary report was presented before the Harvey Cushing Society pertaining to the use of an "Old Non-Surgical Form of Therapy for Trigeminal Neuralgia" (1). This report dealt with the use of ferrous carbonate prescribed in large doses in a series of 15 cases. A knowledge of the reputed usefulness of this medication in the treatment of trigeminal neuralgia had been acquired from a perusal of a book written in 1822 by Samuel Hutchinson, entitled "Cases of Neuralgia Spasmodica Commonly Termed Tic Douloureux Successfully Treated" (2). Innumerable other remedies having been recommended for this malady and generally found ineffective, we first thought that Hutchinson may have been erroneous in his diagnosis and that failure to distinguish between trigeminal neuralgia and other forms of neuritis was responsible for the favorable results he reported with ferrous carbonate. The recorded description of the symptoms suffered by his patients, however, completely dispelled any such doubt. A few quotations from Hutchinson's monograph will convince the reader that the author enjoyed a masterful familiarity with this illness as well as with the pitfalls in its diagnosis.

"The complaint commences with slight and almost imperceptible attacks of pain, and generally without any warning; though some patients feel in the affected part peculiar and

inexplicable sensations preceding its approach, from which they can announce with horror the coming enemy; the patient at the same time enjoying a good or an indifferent state of health. The pain, however, soon becomes more acute and lancinating, shooting and darting along the various ramifications of the affected nerves: it generally continues from a quarter to half a minute, and seldom exceeds the space of one minute. It returns at intervals more or less frequent: there being sometimes several paroxysms in a few minutes: and at other times there are intervals of from fifteen to thirty minutes, or longer. There is no determinate period: we always find the utmost irregularity, even in the same patient.

"The pains vary in their degree of intensity; at one time exciting the most piercing cries, and distracted writhings and motions in the afflicted patient, while at another they are more bearable. When at the acme of their violence, the parts affected are often convulsed, and sometimes various contortions and grimaces are observable. These are to be distinguished from the convulsive twitchings of the muscles with which the diseased nerves communicate, and which are occasioned by irritation from the excessive pain; while the contortions and grimaces are voluntary, being caused by the patient's writhing and twisting from the agony of his torture, and may be prevented by a firm resolution to resist any impulse of shrinking from the attack.

" . . . It rarely gives warning of its approach, and frequently the first sign of an attack is the patient starting up in a state little short of phrenzy. In this condition, some patients beat the parts with violence, or forcibly rub them with some rough substance till excoriation takes place; and in some few instances they have thus succeeded in diminishing the intensity of the pain.

" . . . The pains are more frequent during the day than in the night, probably from there being at this time fewer causes of irritation; and they are more frequent during conversation

than in silence, and still more so at the time of mastication, when the attacks often succeed each other with such rapidity, as to appear like one continued paroxysm, with scarcely an interval of cessation.

" In general only one side of the face is afflicted with this dreadful disorder; but as there are cases recorded in which both sides suffered at the same time, we cannot lay it down as a certain characteristic of the disease.

" When the disease continues for a great length of time with increasing violence, the patient can neither obtain rest by night nor by day: his appetite fails, and, as may be expected, there is some degree of pyrexia: this, however, but rarely happens, and only in cases of the utmost severity.

" Hartenkeil, Hildebrande, Baldinger, and some other German writers, relate cases of what they call *tic douloureux*; which, though in some particulars they resemble that affection, in others differ from it very materially. The first of these writers describes it as having been very prevalent at Salzburg; but the pain was periodical, recurring once in twenty-four hours; often remaining for several hours at a time, and then suddenly departing.

"I should, however, rather suppose these to be cases of hemicrania, which has, in many instances, been observed to attack the patients periodically, and to yield to the bark."

" But those who are familiar with the symptoms of the neuralgia faciei, well know their superior degree of violence, the shortness of the interval between each attack, and the obstinacy with which they resist the generality of remedies opposed to them."

The histories of 21 cases of trigeminal neuralgia in which relief of pain followed the administration of ferrous carbonate are appended in Hutchinson's publication. His prescription was *Ferri carbonatis ʒi fiat pulvis bis die sumendus ex melle, vel theriaca*. While convinced that iron possessed great palliative,

if not curative, powers, Hutchinson admitted that not all cases of tic douloureux were favorably affected. In a postscript, he stated that "the carbonate of iron has, in a few instances under my own cognizance, been inadequate to the difficult task of curing the tic douloureux." He was inclined, however, to attribute these failures "rather to the absence of a due perseverance in the use of the remedy than to any failure in its power."

In 1942, the senior author reported on the use of this medication in 15 patients. Four capsules each containing one gram of ferrous carbonate were prescribed, to be taken twice daily with meals—a total of 8 grams a day. The second and third branches of the trigeminal nerve were jointly involved most frequently although the series also included examples of involvement of single branches, as well as of other combinations. The patients were observed for periods varying from 2 weeks to 12 months. Diminution in the severity and frequency of recurrence of the pain followed the administration of the ferrous carbonate in 12 of the 15 cases. It was noted that the improvement did not begin at once, but after an interval of time averaging 13 days. Disagreeable side-effects were reported by two patients. One complained of nausea, anorexia and diarrhea, the other of constipation.

Since 1942 considerably more experience has been gained in the treatment of trigeminal neuralgia with massive doses of ferrous carbonate. The present report deals with an evaluation of this form of therapy in a series of 91 patients. There were 49 males and 42 females ranging in age from 23 to 79 years. Eighty-five per cent of the cases were between the ages of 41 and 70. The duration of symptoms varied from 1 week to 27 years, with an average duration of 5 years. The branches of the trigeminal nerve most commonly involved were the second and third in combination. Next in frequency was involvement of the maxillary division alone.

In evaluating the results of any form of medical regime, one must constantly bear in mind the fact that the course of trigeminal

neuralgia is punctuated by spontaneous periods of remission. These periods of quiescence may last anywhere from a few weeks to several years, usually becoming shorter as the duration of the illness increases. In so far as it was possible to do so, the merits of the iron therapy were decided upon in the light of the course and duration of the spontaneous remissions in each particular case. Of the 91 patients submitted to this form of treatment, fifty-seven failed to obtain any appreciable relief. Several patients who seemed to respond favourably for a few weeks only are included in this category. Thirty-four patients or approximately one third of the series were benefited by the ferrous carbonate. This group consisted of 16 males and 18 females, varying in age from 23 to 72 years. Twenty-eight of the 34 patients were in the fifth, sixth or seventh decade of life. The duration of symptoms varied from 4 months to 27 years, averaging 6 years for the entire group. The maxillary and mandibular branches were jointly involved most frequently. Complete relief of pain was achieved in 3 cases for periods of 11 months, 13 months and 7 years. The two patients relieved for 11 months and 13 months respectively suffered recurrences which eventually led to operation in one of them. In 24 cases the use of the medication resulted in considerable improvement, while in the remaining 7, improvement of a moderate degree was achieved. The improvement has lasted for periods varying from 6 months to 6 years. Seventeen patients suffered a severe recurrence of pain which eventually led to operation in 11, while another 3 required alcohol injection. It is perfectly possible, of course, that as more time elapses, an additional number of patients will require surgical intervention.

The improvement observed following the administration of the ferrous carbonate usually occurred about one to two weeks after the institution of therapy. It varied between the extremes of 2 days and 6 weeks. Intolerance to the medication manifested by nausea, vomiting, diarrhea or constipation occurred in a few instances. Omission of the drug for a few days, graduated dosage, the use of liquid petrolatum to deal with constipation, and in-

sistence that the capsules be taken with meals usually corrected these side reactions. Two patients in our experience, however, were wholly unable to tolerate the medication and are not included in this study.

The following case reports are illustrative of the course of events following the administration of ferrous carbonate in which improvement resulted:

Case 1. A 61 year old manufacturer was originally seen in July, 1940, complaining of recurrent attacks of shooting pain in the distribution of the left upper lip of many years' duration. Occasionally the painful paroxysms involved the whole left side of his face. His symptoms could be initiated by shaving, chewing and washing with cold water. Periods of remission lasting as long as 2 or 3 years had occurred in the past, but recently these periods during which he was free from pain were of much shorter duration. He had been subjected to a variety of therapeutic procedures, including extraction of teeth, alcohol injections, parenteral administration of vitamins, and diathermy. None of these measures afforded him relief. Accordingly, in August, 1940, section of the sensory root of the left trigeminal nerve was performed, following which he was completely relieved of his old pain. In October of the same year, he began to complain of a similar pain on the right side in the supra-orbital and malar regions. There was a demonstrable trigger zone. Injection of the supraorbital and infraorbital nerves with alcohol resulted in an abolition of pain for over a year. In February, 1942, he experienced a return of the painful paroxysms and in May, the alcohol injections were repeated. His symptoms did not abate, however, and on May 26, 1942, treatment with ferrous carbonate was begun. Two days later he was free of pain. He has been followed for a period of 7 years, and except for an occasional twinge of pain in 1944 when he reduced the quantity of his medication, has remained asymptomatic. In 1946, he reported that he was taking 2 grams of ferrous carbonate daily and in 1948 he discontinued its use entirely. He was last heard from in March, 1949, at which time he had no pain whatsoever.

Case 2. A 40 year old clerk came under observation in July, 1944, because of pain in the right side of the face for a period of 2 years. The pain which was likened to a series of electric shocks was felt in the center of the cheek, the angle of the mouth and occasionally about the chin. It occurred in paroxysms which could be precipitated by talking, chewing, shaving or washing the face. Touching the upper lip set off an attack. He had experienced several such episodes in the past 2 years, the most recent one having already lasted some six weeks. Previous treatment, which consisted of novocaine and alcohol injections and inhalations of trichlorethylene had been ineffectual.

The neurological examination disclosed no abnormalities. Treatment with ferrous carbonate was started and after five days, he felt considerably improved. He has been followed for a period of 4 years, during which time he has continued to take his medication. Occasional mild attacks of pain of 3 or 4 days' duration do occur, but these are bearable and do not incapacitate him. In March, 1948, he estimated that he was about seventy per cent relieved.

Case 3. A 52 year old retired manufacturer first applied to this clinic in June, 1939, for relief of pain involving the right malar region. The pain, described as shooting in character, had been intermittently present for a period of 2 years. Operation was advised but rejected by the patient. An alcohol block was then performed at another clinic, which gave him partial relief for about 2 years. In March, 1942, he reappeared, his pain having become much more severe. Ferrous carbonate was prescribed and after an interval of 3 weeks, his pain began to subside. For a period of almost 3 years during which he continued to take his medication, he remained almost completely free of any discomfort. In January, 1945, severe pain recurred in the distribution of the maxillary and mandibular divisions, which yielded only to differential section of the sensory root of the trigeminal nerve.

Case 4. A 70 year old male patient was seen in August, 1938, complaining of severe paroxysmal pain within the distribution of the left supraorbital nerve. The pain had been intermittently present for 7 years. An alcohol injection into the nerve was performed which gave him relief for 2 years. In July, 1940, the sharp, stabbing pain recurred and in September of that year, the supra-orbital nerve was avulsed. Pain disappeared to return again in April, 1942, at which time ferrous carbonate was prescribed. Within 2 weeks, improvement was evident. He still experienced occasional twinges of pain, but their severity was considerably less. In February, 1943, he discontinued taking the medication, pain having left him entirely. A recurrence of symptoms followed, which was again relieved by ferrous carbonate. In June, 1943, pain referable to the right supraorbital nerve appeared, which persisted until November, 1943, when an alcohol injection was performed. Since then he has only occasionally experienced slight pain. He continued to take the medication until January, 1948. When last heard from in August, 1948, he was free of pain.

Through the kindness of Dr. S. Granick of the Rockefeller Institute of New York, determinations of the serum iron content were carried out in 18 patients. While the results were not conclusive, there appeared to be a tendency on the part of patients with trigeminal neuralgia to show a serum iron content somewhat higher than normal, regardless of whether the determina-

tions were done prior to or after taking ferrous carbonate. One cannot presume to interpret these results either from the etiologic or therapeutic point of view.

COMMENT

Our experience with this form of treatment does not justify the degree of enthusiasm accorded it by Hutchinson. From the data which have been provided, it is clear that only a small proportion of patients derive lasting improvement from it. In this respect, Hutchinson's claims do appear extravagant. One fact, however, does emerge from this study, which we believe has significance. An appreciable number of patients, approximately one third in our series, were benefited, though admittedly the improvement was frequently not sustained indefinitely. These patients were often still subject to occasional twinges of pain, but their discomfort was relatively mild, the pain being quite tolerable. Compared with the results following section of the sensory root, our claim for the usefulness of ferrous carbonate is indeed a modest one. It must be realized, however, that it is not the intent of the authors to advocate this method of treatment as a substitute for surgery. The treatment of choice for trigeminal neuralgia is unquestionably section of the posterior nerve root. It is suggested, however, that in cases in which operation is rejected or deferred for one or another reason, ferrous carbonate be given a trial. A certain number of patients will be relieved, the duration of the improvement being variable. Of these, some may be relieved indefinitely. There is no way of telling beforehand which patients will respond favorably.

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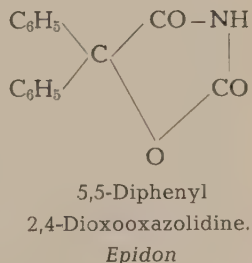
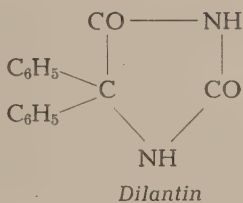
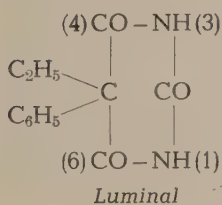
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Further Experiences with Epidon and some Experiments with Other Anticonvulsant Drugs

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A new anticonvulsant drug 5,5-diphenyl—2,4-dioxooxazolidine (*Epidon*) was mentioned in earlier publications (2, 3: 1947). Its chemical composition in relation to other antiepileptic remedies, is as follows:



Clinical experiences in the use of *Epidon* have been reported by Kobbernagel (7. 1948). In order to outline the limits for the future use of *Epidon* as an antiepileptic drug, I shall briefly report some cases, two of which have been followed up from my first publications.

No. 1. A 41 year old furrier, admitted to Sct. Hans Hospital in 1936 and Mar. 28th to Dec. 15th 1945. Diagnosis: Essential epilepsy. Intellectual inferiority (with hysterical reactions). Epileptic fits since 1930, several times admitted to different Copenhagen hospitals. Neurological examination, spinal fluid, X-ray of the skull: normal.

Mentally he was at times querulous and hysterical in his behaviour and showed evidence of intellectual inferiority. Occasionally he was docile and cooperative.

A large number of fits in July 1945 left the patient with some mental torpor. The patient was submitted to Epidon treatment (4.8 g daily) and luminal dosage gradually diminished. The result was a prompt reduction of the number of attacks. Mentally he improved strikingly, being alert without signs of torpor, quiet and friendly. After discharge in Dec. 45 the patient has pointed out that he does not feel sleepy and heavy, as was the case with the luminal-diphenylhydantoinate treatment.

Dosage until October 48: 4.0-3.2 g Epidon daily. No toxic effects. Frequency of fits: one (not very pronounced) fit every three months. Later the dosage has been gradually decreased to 1.6 g a day, but occasionally raised, when working hours are longer. Two severe fits in November 48, one in May 49 (follow-up 15th May). The patient has been able to work and put in overtime as a furrier, later on as a workman in heavy industrial factory.

No. 2. 52 year old woman translator. Diagnosis: Diffuse cryptogenetic atrophic encephalopathy. Neurological dept. of the University Hospital (Rigshospitalet) 1941: Encephalography: diffuse very pronounced symmetrical internal hydrocephalus. Spinal fluid, X-ray of skull, ophthalmoscopy: normal. Wassermann reaction: negative.

Since 1941 epileptic fits. Once in 1941 postparoxysmatic paresis of right leg and right-sided ptosis. Since Febr. 1946 Epidon 3.2 g a day. Follow-up in Feb. 1949. One major fit every one to two months. One narcoleptic fit a month. The patient tried for a prolonged period to reduce the Epidon dosage to 1.6 g daily. The frequency of fits increased to two major fits a month and one narcoleptic fit every week, as a result of which the first dosage was resumed. She felt better during Epidon medication, did not become sleepy as on previous luminal-diphenylhydantoinate dosage. She was able to carry on her profession, which had not been possible before.

No. 3. 7½ year old girl. Diagnosis: Essential epilepsy. Jan. 1946: 3 major fits, later by minor fits only. In April 47: 50-60 minor fits daily. Neurological examination and X-ray of skull: normal. Treatment from April 47 with Epidon 1.2 g + Tridione 0.5 g daily, after which minor fits entirely ceased.

Tridion dosage gradually decreased, from June 48 only 1.2 g Epidon daily. Since then three abortive minor fits (follow-up April 49). No toxic effect.

The child has been able to attend kindergarten and school, which previously she did not.

No. 4. 24 year old engineering student. Diagnosis: Essential epilepsy. Since 1941 major epileptic fits. Frequency per year: 1942-1945 increasing from 9 to 31; the subsequent years: 40-50.

Neurological examination (Dec. 48): normal, except for slight convergent strabismus and moderate deafness. Encephalography: very pronounced symmetrical internal hydrocephalus. Spinal fluid: normal. Wassermann test: negative. Electroencephalography: strong general dysrhythmia most pronounced on the left side. Arteriography: normal.

The patient had previously been treated with phenemal-diphenyl hydantoinate with only slight reduction in frequency of fits and increasing mental torpor, so that he was unable to carry on with his studies. Epidon treatment from January 48: 4.8 g daily + luminal 0.2. Frequency of fits was markedly reduced and the patient improved mentally, so that he was able to resume his studies. Jan.-April 49: 2 major fits.

To get an impression of the effect on outpatients some reports from general practitioners were obtained.

TABLE I.
Number of cases: 14

Age	5-20	21-40	41-55	67
Number	3	8	2	1

Diagnosis:

Essential epilepsy	8
Traumatic epilepsy	3
Atrophic processes	2
Cerebral arteriosclerosis	} 1
Cerebral thrombosis	

Period of Epidon treatment:

Months	2	3	6	6-11	12	18-20	24
Number	2	1	1	3	3	3	1

13 patients previously treated with phenobarbital or diphenylhydantoinate.

Effect of Epidon medication:

(with or without phenobarbital 0.10)

Working capacity improved	5
Frequency of fits diminished	5
" " " as before	3
Reported effect on minor fits	3

From these series it might be concluded that the Epidon in certain cases has some effect even on the minor fits. Patients who should benefit from Epidon treatment may be selected in this way:

- (1) cases suffering from the hypnotic or toxic effect of phenobarbital or the toxic properties of diphenylhydantoinate;
- (2) cases with a not too long history of fits, thus excluding most cases of the institutionalized group,
- (3) cases with only slighter mental disturbances, if any.

In this way we possibly reach a smaller group of patients, living outside hospitals, studying or earning their living by their own work.

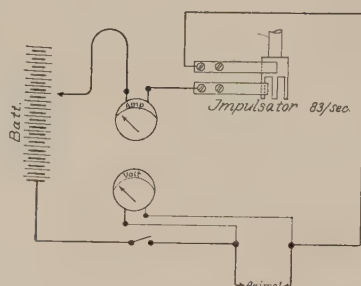


Fig. 1.

Trying to find a drug with still better anticonvulsant properties the following compounds were studied. The experiments were all carried out in the Lundbeck factory research laboratories, and all the compounds used were synthesized by the chief chemist P. V. Petersen.

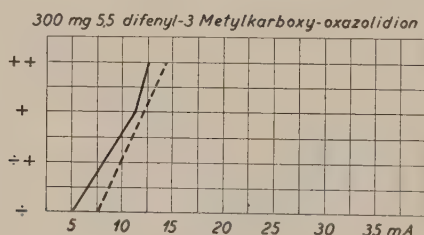


Fig. 2.

Rabbit. — before administration.

----- 2. h. after intravenous administration.

To study the anticonvulsant properties a modification of the method described by Merrit & Putnam (6. 1937) for determining the threshold for convulsiones was used (Fig. 1).

One electrode was placed in the mouth against the palate, the other on the shaved convexity of the cranium. The current was measured by a milliammeter in the circuit and was varied by shifting from one element to the next (each of 1.5 volt). For

each determination the current was applied for a period of 5 seconds. If no convulsions resulted after a 3-minute interval, a current 1.5 volt stronger was administered. The convulsive

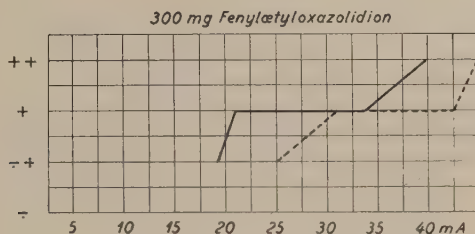


Fig. 3.

Rabbit. — before administration.
 ----- 2. h. after intravenous administration.

threshold for untreated animals was determined twice or three times a day, with two- or three-hour intervals between tests.

In registering the results the initial, but not generalized, convulsions are labelled as + —, generalized convulsions +,

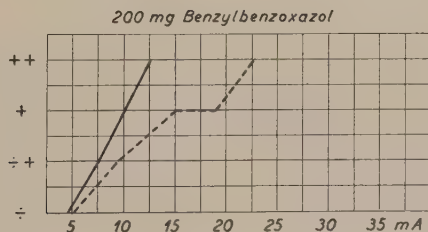


Fig. 4.

Rabbit. — before administration.
 ----- 2. h. after intravenous administration.

and very severe convulsions, with more or less rotation of the animal, + +.

The first compound as well as the second and the third was made in the Lundbeck factory for the first time: 5-5-diphenyl-N-methyloxazolidinedione. This compound proved to be quite insoluble, and a suspension was so difficult to make that experiments with injections were given up.

The second compound: the 5-5-diphenyl-3-methylcarboxy-oxazolidinedione, is insoluble, but the sodium salt is soluble in water (Fig. 2).

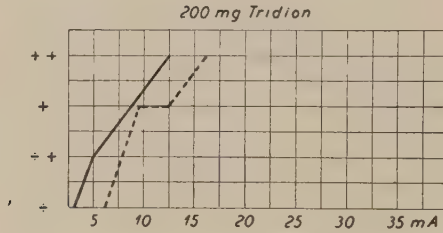


Fig. 5.

Rabbit. — before administration.
 ----- 2. h. after intravenous administration.

It has been administered intravenously to rabbits in 300 & 400 milligram doses, but shows a much less effect than Epidone.

The third compound: 5-5-phenylethyl-oxazolidinedione, as the latter insoluble, but the sodium salt is easily dissolved. Intra-

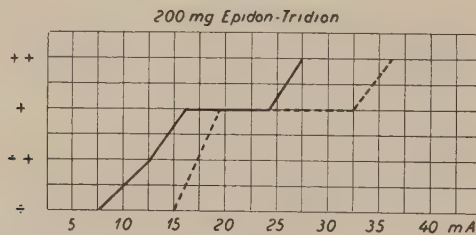


Fig. 6.

Rabbit. — before administration.
 ----- 2. h. after intravenous administration.

venous administrations to rabbits has shown very toxic effects, the animals being nearly comatose and developing a paresis of the hind limbs. A 100 milligram dosage produces only a small anticonvulsant effect, and a 200 milligram and especially a 300 milligram dosage gives a definite effect, but difficult to judge, on account of the very intoxicated state of the animal (Fig. 3).

The fourth compound because of its chemical formula does

not quite belong to this series, but had to be checked against the reports of Bywater, Coleman, Kamm & Houston Merrit (1. 1945).

The 2-benzyl-benzoxazol is an oil quite insoluble and does not

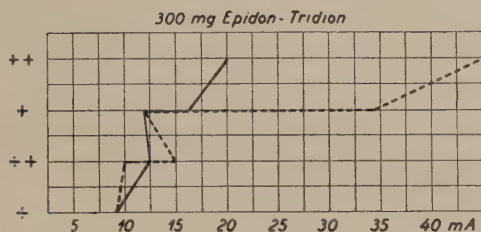


Fig. 7.

Rabbit. — before administration.

----- 2. h. after intravenous administration.

form any salt. 200-300 milligrams intramuscular dosage on rabbits show only a moderate effect (Fig. 4).

The fifth compound. 3-ethyl-5-5-dimethyloxazolidinedione is easily dissolved in water. As clinical experiments have been

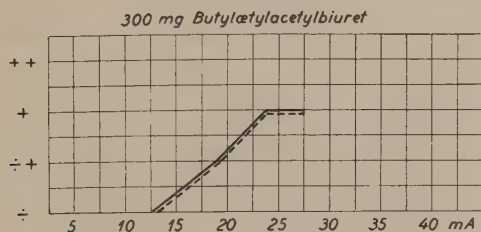


Fig. 8.

Rabbit. — before administration.

----- 2. h. after intravenous administration.

carried out by other authors no mention will be made here.

The sixth compound is at the present time very well known, the *Tridione* 5-5-methyl-N-methyl-oxazolidinedione.

To combine its strong effect against minor fits with the Epidone effect against the major attacks, we tried to make a chemical combination of these two compounds by means of ethan, a task that proved impossible to perform. A direct mixture of the two

compounds in a great number of series showed only a marked anticonvulsant effect of the Epidon,—it was administered intravenously to rabbits in 200-300 milligram doses (Figs. 5-7).

The seventh compound: 5-5-dimethyl-2-tion-4-oxo-oxazolidine is easily dissolved in water. 300 milligrams intravenously administered to rabbits produced a moderate anticonvulsant effect. A greater dosage caused paresis a few times, but it remains uncertain if this effect might be considered as toxic.

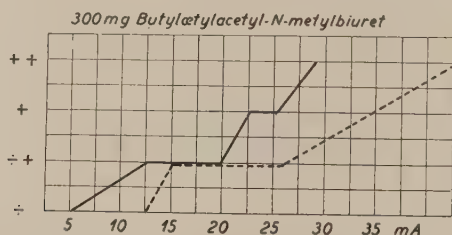


Fig. 9.

Rabbit. — before administration.

----- 2. h. after intravenous administration.

As this compound, however, has a very definite effect on the thyroid gland, very much alike the tiouracils, we dropped further experimentation.

The eighth compound together with the ninth, for the first time synthesized by the L.f. 5-5-3-trimethyl-2-tion-4-oxo-oxazolidine, is insoluble. 200-300 milligrams were given intramuscularly to rabbits with practically no effect.

The ninth compound, 5-5-diphenyl-3-fenyl-oxazolidinedione, is so completely insoluble that no anticonvulsant experiments have been performed.

From these experiments the conclusion may be drawn that in this series of oxazolidinediones, tridion, didion, and epidone are the only valuable compounds in the treatment of epilepsy, as either the chemical properties of the other compounds do not allow them to be used or their anticonvulsant effect is too small.

In our search for anticonvulsant drugs we tried to find other series of compounds containing the CONH group twice. On the

basis of the paper of Hill & Degnan (1940) and of Hamilton Anderson & S. Y. P'an (1941) about the hypnotic effect of a series of dialkylacetylbiuretes we tried to determine whether there were any anticonvulsant properties in these compounds.

The toxicity of these compounds is very low. It should be remembered that the so-called hypnophore group is present here, just as in the barbiturates.

The first compound was produced for the first time by the American authors. It is 1-n-butylethyl-acetyl-biuret. It is comparatively insoluble, but the sodium salt is easily dissolved.

It has been administered perorally as 50 milligram in powder-form to guinea pigs without any anticonvulsant effect. The sodium salt has been given intravenously as 300 milligram to rabbits, also without effect (Fig. 8).

The second: 1-n-butyl-ethyl-acetyl-5-methylbiuret has for the first time been synthesised by the L.f. Like the first, it is insoluble, but forms soluble alkali salts. It has been administered in powder form to guinea-pigs.

Of the sodium salt 300 milligram was given intravenously to rabbits with a marked effect, although slightly less than that of Epidon. The better effect must be considered due to the alkylation of the 5-carbon-atom (Fig. 9).

As the toxicity of these compounds is very low, it seems possible that an antiepileptic drug may be found here. However, the synthesis is even more difficult and expensive than that of Epidon, and therefore further development seems barred.

The last one, 1-n-utyl-ethyl-acetyl-5-fenylbiuret, also for the first time synthesised by the L.f., is insoluble and cannot form alkali salts. In powder form peroral doses of 50 and 100 milligrams had no effect on guinea-pigs.

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On "Cataplexy" in a Case of Frontal Lobe Tumour

By
SVEN ETHELBERG

Though so-called cataplectic attacks without additional narcolepsy have been reported previously (Berliner and Schilder 1926, Rotfeld 1928, Redlich 1931, and others) their occurrence in intracranial tumors seems to be so rare and their genesis so obscure as to make the report of the following case defensible.

Case report (AKH-G-5658). To the Neurosurgical Department, Aarhus, a woman of 54 was admitted, who for about twenty years had suffered from sudden and violent attacks of headache of a short standing (10 minutes) and only once or twice a year. The attacks were usually associated with unsteadiness of gait with a tendency to deviate to the left. And she had occasionally lost consciousness. Besides these she had experienced sudden and rapidly transient accesses of muscular weakness or limpness. The latter form of attack lasted varyingly from a few seconds to a few minutes and they occurred for many years only twice or three times a year. But for the last months they had been increasingly frequent, the intervals ranging from hours to days. The limpness was more marked in the legs than in the arms. When standing or walking she would sag at the knees but never fall down. When possible she would sit down. The arms also went limp and would sink down and there was a slight relaxation of her grasp. During the attack she was unable to move and to utter a sound. She had noticed that the attacks occurred perhaps a little more common when she was cycling. In that case she was able to get down without falling. Though the attacks thus possibly were precipitated by physical exertion she knew nothing of other eliciting factors, in particular they were never induced by strong emotions, neither laughter, anxiety nor crying. During attacks she was completely aware of what happened; there was no drowsiness nor any blunting of consciousness. She denied the presence of giddiness and vertigo. For the last three months another variety of attacks

supervened, viz. clouding or loss of consciousness of a short standing—from one to a few seconds—in both cases she would fall down. They were occasionally initiated by a loss of muscular tone as described above, followed by blunting of consciousness and fall. On other occasions the loss of consciousness was initial. Both forms might be associated with incontinence of urine. Recovery was rapid and complete in both. For about six months her memory became poor, a definite lack of initiative developed and she was always in a depressive state of mind. For one and a half months she had experienced obscurations and scotomas in both visual fields.

Examination. She was oriented as to time and place and perhaps a little sluggish though not definitely somnolent. A marked lack of attention was disclosed clinically and by test, in striking contrast to the good performance of retention-recall test. There were a marked hypomotility and lack of initiative. She was lying inert in bed for hours, though completely awake. The general feeling tone was shallow. Occasionally she was a little euphoric, but no marked facetiousness was observed. She co-operated willingly. Slight choking of both optic discs. No loss of motor power. Questionable spasticity and increased deep reflexes in the left-sided extremities, the latter more marked in the leg. No Babinski response, no fanning sign. The gait was unsteady and tumbling. The Romberg test showed falling backwards and to the left. Blood pressure: systolic 140 and diastolic 90. Wassermann reaction on blood negative. Lumbar puncture was not performed. Electroencephalography showed slow waves corresponding to the upper part of the right premotor and prefrontal regions. Roentgen-examination of the skull normal. Ventriculography disclosed a slight displacement downwards of the right anterior horn and a more marked displacement to the left of the left anterior horn of the lateral ventricles. Right-sided angiography could not be completed.

Operation. (Ethelberg). An osteoplastic flap was reflected exposing the anterior part of the superior mesial border of the hemisphere. Localized between the mesial surface of the frontal lobe and the falx the extracerebral part of a soft, richly vascularized tumour was found (cf. fig. 1). The tumour made a definite impression on the cortex and the genu of the corpus callosum, affecting the anterior part of the cingulate gyrus—Brodmann's area 24—and further the entire area 32 and the lower mesial parts of areas 8, 9, and 10. This part of the growth was removed by suction. It was supplied by an abnormally enlarged branch from the anterior internal frontal artery (from the anterior cerebral artery). Just anterior and lateral to the genu of the corpus callosum the tumour was intracerebral, confined by the basal ganglia laterally and by the mesial and orbital surfaces of the frontal lobe. Complete removal of the goose-egg-sized tumour.

Microscopy (Dr. E. Christensen). Typical oligodendroglioma. Marked vascularization of the extracerebral part which is the site of numerous small cystic degenerations and oedematous foci. The cortex adjacent to the extracerebral part showed a marked atrophy of the nerve cells and some changes

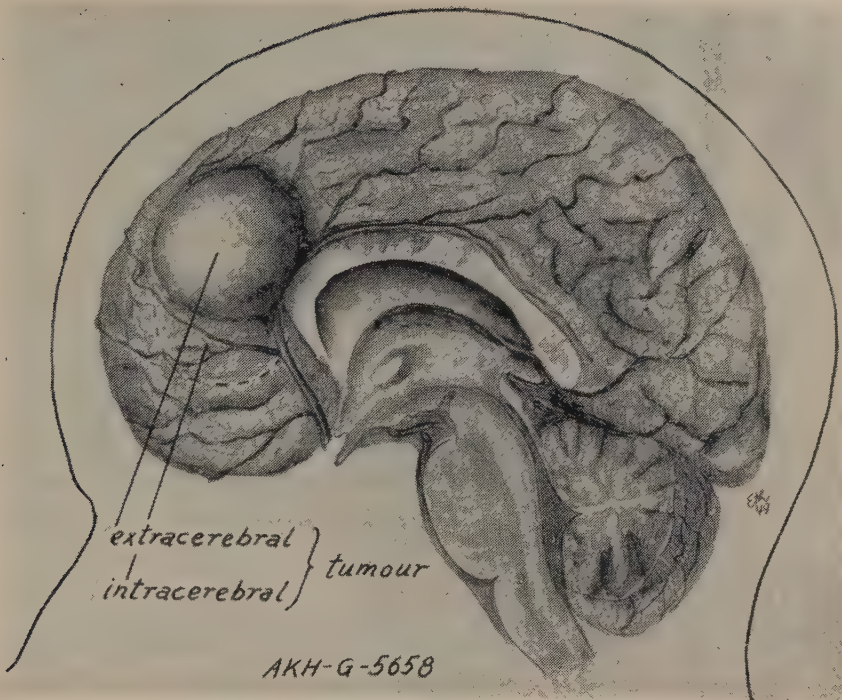


Fig. 1.

Drawing after operation sketch showing the extension and localization of extracerebral and intracerebral parts of the oligodendroglioma.

of the fibers in the subcortical white matter. There was proliferation of glia and neoplastic changes of oligodendroglia scattered among atrophied nerve cells. And, finally, there was a definite decrease in small vessels in the cortex.

Postoperative course. The first 4 days after operation she was a little sluggish and deteriorated. A rise in systolic blood pressure to 180 mm was observed for several days. Subsequently blood pressure fell to normal levels. She became co-operative and oriented again. The emotional state was as before operation. On the 10th day, the day of discharge, she had a "cataplectic" attack with fall and some clouding of consciousness and incontinence of urine.

The main reason for drawing attention to the present case is that some features may have bearing upon the genesis of, at least, symptomatic cataplexy. In summing up these features we find, in the first place, the occurrence for many years of cataplectic attacks without impairment of consciousness and without elicit-

ing emotional factors. In the course of events disturbances of consciousness, varying from clouding to loss of consciousness, supervened. In the second place, the absence of narcoleptic or hypnoleptic symptoms is striking in face of the long history. And, finally, it was possible to localize the cerebral lesion with some degree of precision and to disclose pathological changes of both the nerve cells and the vascular supply to the cortex.

The considerations as to the genesis of the cataplectic attacks have, on the one hand, been concentrated upon disorders of sleep, on the other, upon cerebral processes similar to those resulting in epilepsy. The former view is held by Adie (1926) who, due to the common coexistence of cryptogenetic narcolepsy and catalepsy, considers the latter a specific disorder of sleep, viz. a localized sleep of the centres of movement and posture. The latter hypothesis has been put forward by Wilson (1940). He believes that in the case of catalepsy impulses do not excite, but inhibit the function of the nerve cells in the motor cortex only, other areas being intact and consciousness consequently preserved.

Since in the present case no narcoleptic symptoms developed it would be hard to explain the loss of tone in terms of sleep disturbances. There was nothing, clinically or operatively, indicating involvement of the floor of the third ventricle in the morbid process. On the other hand, there seem to be several points in favour of the latter view, that is to say, that abnormal irritation of a circumscribed cortical area leads to intermittent inhibition of movements, i.e. an inhibitory epileptic attack. The pathological changes, viz. the decrease in number of the small cortical vessels and atrophy of the nerve cells, are generally assumed to be the pathological correlate of inadequate circulation of the area. A varying degree of hypoxia may occasionally lead to a state of neuronal irritability resulting in abnormal uncontrolled discharges (Bronk, 1938). In this respect the pathological and pathophysiological changes are similar to those found for instance in parasagittal meningiomas, affecting the motor region and resulting in Jacksonian fits. In the latter

the spread of discharges is now by Penfield (1941) assumed to depend on descending subcortical connections. When the spread is limited to some extent, the usual focal fit is unassociated with loss or blunting of consciousness. Only when the spread of discharges is generalized unconsciousness supervenes. Whereas the pathophysiological sequence of events and the gross features of their anatomical substratum is relatively well-known as far as the motor region is concerned, we are in a far less favourable position, when the mesial regions of the frontal lobe are to be considered. In recent years, however, experimental neurophysiology has thrown light upon some of the changes ensuing from ablation and abnormal irritation of some parts of the mesial surface. The cortical lesion is, in the present case, confined broadly to Brodmann's areas 24, 32, and the lower mesial parts of areas 8, 9, and 10. Areas 32, 10, and 9 have not in experimental animals yielded motor responses of any kind. But in the monkey and the chimpanzee McCulloch (1944) has shown that irritation of area 8 and even more of area 24 results in relaxation of all somatic muscles, holding in abeyance of motor after-discharge and in suppression of motor response to stimulation of any motor focus of the sensory cortex. Similar phenomena result from stimulation to certain definite cortical areas besides the above, viz. areas 4s, 2 and 19, all of which have been termed suppressor areas by McCulloch. The two former phenomena appeared and disappeared rapidly, while the last response was of a longer standing. As to area 24 these findings have recently been corroborated by Smith (1945) and Ward (1948). McCulloch demonstrated that the suppression of motor response depended upon a descending system, not involving the caudatum, and Ward found evidence of a descending pathway from area 24 to the reticular formation in the mesencephalon.

It would, in my opinion, be no remote possibility to assume that cellular hypoxia, leading to abnormal irritability of the neuronal elements in the area affected, would result in abnormal discharges from area 24 and possibly also area 8, the immediate

consequence of which would be loss of muscular tone and inability to move for a varying, short period of time. Consciousness would be unimpaired until the uncontrolled discharges increased to such an extent that, besides being conducted along normal subcortical pathways, they would "fire" contiguous cortical areas, irrespective of the presence of cortico-cortical connections. That the "firing" of contiguous areas may occur has been shown by McCulloch, when self-sustained discharges appear and even where the cortical areas are functionally disparate and after cutting of the subcortical white matter. It may eventually affect the entire cortex. I believe it is reasonable to assume that this abnormal cortical spread may account for the development of a varying degree of clouding or even loss of consciousness.

In the sequence of events outlined above there seems to be so much conformity as to clinical, pathological and experimental pathophysiological features that it cannot be entirely disregarded. The case is different with the so-called cryptogenic cataplexy. The latter differs from the present case in that the precipitation by emotional stimuli is one of its outstanding characteristics. To assume, at the present time, a similar pathogenesis in cryptogenic cataplexy would be merely conjectural; but of course it cannot be precluded.

Accesses of rapidly transient loss of muscular tone are probably more common than appears from the reports in literature. Without emphasizing their cataplectic nature, David and Askenasy (1937) report sudden, universal, hypotonic attacks in an ethmoidal meningioma. And the present author has been able to demonstrate cataplectic attacks without impairment of consciousness in one ethmoidal meningioma and two meningiomas of the falx of the anterior group (material in preparation). These growths affect the cortex even more exclusively than does the kind of tumour reported here. The ethmoidal meningiomas extend upwards between the frontal lobes, lying in intimate contact with both mesial surfaces, and the anterior group of falx meningiomas affect from the onset of growth both anterior limbic areas directly.

SUMMARY

The author reports a case of oligodendroglioma of limited extension, affecting the cortex of the mesial surface of the right frontal lobe. The tumour was both intracerebral and extracerebral. The cortex underlying the extracerebral part was the site of atrophic changes of the nerve cells and the number of small vessels was considerably diminished. The patient had suffered from accesses of loss of muscular tone for a period of twenty years; first unassociated with impairment of consciousness, later clouding and loss of consciousness supervened. No emotional, eliciting factors could be disclosed and no narcoleptic symptoms developed. The pathogenesis of the attacks is discussed in the light of recent experimental investigations. *The author is inclined to conceive of these attacks of "symptomatic cataplexy" as inhibitory or suppressive epileptic fits, in no way differing, in essence, from other focal types of the epilepsies.*

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On Crossed Associated Movements

By

MOGENS FOG

The term: associated movements has been applied to a great variety of synkinesias occurring under pathological conditions, homo- as well as heterolaterally, under intended as well as under unintended movements. In the present study the term is confined to denote those involuntary contractions, which may be elicited in one extremity under purposive action of the corresponding opposite limb.

The characteristics of these symptoms are: (1) that they occur most constantly and pronounced in hemiplegias, which arise in early life, i.e. infantile hemiplegias, (2) that they appear preponderantly in the paretic limb under intended movements of the intact extremity, (3) that they are especially distinct and differentiated in the peripheral muscle-groups, (4) that the movements are mostly homologous to—"imitating"—the primary contraction, and finally (5) that they are influenced by tonic labyrinthine and neck reflexes (Walshe 1923).

These facts have often been stated, but in my opinion some features of the symptomatology have not been sufficiently emphasized, features which may throw new light upon the pathophysiology of the phenomena.

The following observations are based on the study of normal new-born, infants and adults, and on examination of fifty patients

suffering from infantile and late hemiplegias. As the signs are most explicit in the upper extremities, only these are taken into consideration.

—As already mentioned, infantile hemiplegias are inclined to present crossed associated movements more constantly and on a much less energetic voluntary contraction than is the case of paresis developed in later years. The tendency to contralateral synkinesias, when first acquired during childhood, is maintained throughout life.

The involuntary movements of the paretic limb present a fairly close relationship in time and direction to the intended contraction. Especially are purposive actions of the unaffected hand and fingers followed by prompt and nearly identical contractions of the corresponding muscles. The more inexperienced the action performed, the more pronounced is the associated movement. On stronger innervation the synkinesias will attain a more athetose-like character and this holds true in the first place of movements in the elbow and the shoulder-joints.

It is not infrequent to observe a cooperation of the unaffected hand, when the patient tries to use his paretic extremity. These movements also bear a close resemblance to that intended, but they never change into athetosis.

When crossed synkinesias appear in individuals who have acquired their hemiplegias in adult years, they are less differentiated and frequently occur on lower thresholds of stimulation in the unaffected limb than the paretic extremity. Also, they are often confined to the proximal parts of the arm and may take the opposite direction of that produced by the hemiplegic extremity.

As a whole crossed movements are rare in these cases. They may, however, be elicited more frequently than generally noticed, if complicated and distinct actions are required. Closing of a safety-pin by means of two or three fingers of the healthy hand, for instance, will often cause homologous cooperation of the paretic side, even in patients who do not present this sign

on usual stimuli. These reactions are quite similar to those met with in infantile hemiplegias following simple performances.

Crossed associated synkinesias are not confined to pathological conditions. If a man, not trained for skilled activities with his fingers, is induced to close a safety-pin in the way mentioned, he will often move the corresponding fingers of the opposite hand. This is invariably the case in children of less than 8-10 years. Most adults who start learning some unusual and complicated performance with their hand, for instance taking a match out of the box and lighting it by use of one hand only, will present slight or pronounced similar crossed action, the piano-player to a less degree than the farmer. There is a predominance of the right hand to cooperate when the left is at use.

If these phenomena are compared to the behaviour of the young infant, obvious resemblances are disclosed. Before the fifth month the baby is unable to produce one-hand action (Bühler). Whether the grasping reflex is elicited on stimulation of one palm, or a one-hand grasp is intended (which begins about an age of four months), the opposite fingers will generally contract. With six months it is possible to evoke an isolated grasping *reflex* on one side, but when the child clenches one hand *on purpose*, the other will often at the same time produce a grasping movement. This may have a pseudo-voluntary appearance. For instance: The infant reaches for an offered finger and simultaneously crumples up the carpet with the other hand. During the last half of the first year this cooperation is abolished.

Steinmann (1931) has investigated children with retarded mental development. She finds associated movements more frequent and more conspicuous than in normal individuals of the same age, their degree depending on the state of retardation. She also emphasizes that they arise especially during inexperienced movements and that they decrease, when the child grows older.

When both hemispheres are damaged in early life, associated movements are often extraordinarily dominant and precise. They

may be present even if there does not remain or never existed any sign of paresis. One of my patients, a man of twenty-one, had a history of a prolonged delivery with asphyxia and retarded development of all somatic functions. His only complaints were of strong and homologous synkinesias. Apart from a double Babinski sign no other neurological symptoms could be revealed.

—The outcome of these observations seems to be that pathological crossed associated movements are the expression of some normal primitive mechanism. There is a gradual transition from the double-handedness of the newborn to the associated contractions in older children and adults under performance of inexperienced actions, when the most differentiated movements of hand and fingers are involved. A transition, further, to the well-marked contralateral activity of paretic limbs in infantile hemiplegias and finally to the more indistinct and inconstant phenomenon in patients who have not acquired a cerebral damage until after full maturing of the central nervous system. The sign is specially pronounced in those discrete movements, which are primarily excluded from cerebral control in hemiplegia.

Crossed associated movements must be indicative of reduced or undeveloped cortical inhibition. The question arises, however, through which mechanism they are produced. Walshe in his classical study claimed that the synkinesias are tonic reflexes, originated by proprioceptive stimuli from the muscles in the unaffected side during intended action. This conception he bases on the long latency period which he observed, and on the well demonstrated influence of labyrinthic and neck reflexes. Walshe seems to have studied especially cases of adult hemiplegias under strong stimulations. My object has been the distinct reactions of the contralateral fingers, which are closely related in time to the intended movements, and which present a more or less precise similarity to voluntary action. It is unlikely that the cortical inhibition should be transmitted through subcortical centres of an undisputedly less differentiated character, to muscle-

groups which at least in later years play an unimportant rôle in the maintenance of posture.

There is, no doubt, a difference between the discrete co-movements, which I have described under normal and pathological conditions, and the cruder synkinesias, which Walshe observed, and which I, too, have noticed in adult hemiplegias. The distinction, however, is apparently not absolute. As mentioned, I found minor associated activity converted into twisting, athetose-like movements also in cases of infantile cerebral damage, when the voluntary innervation became strong.

It would be premature to venture on any conjectures as to the intimate interaction between cortical and subcortical structures deciding normal inhibition of contralateral activity. Only it seems justified to call attention to the integrative balance of stimulation and inhibition, which is exerted by the motor areas 6 and 4, including 4 s (Hines). A damage—or immaturity—of these areas and their connections might count for the observations dealt with in this study.

With all the modesty due to an interpretation based only upon clinical phenomenology, the following conclusions are presented: Impulses to voluntary action in early infancy arise or spread through both hemispheres. On maturing of the cortex and on training in detailed performances, the impulses are more and more lateralized and limited, probably because of inhibitory functions. Inexperienced, complicated activity also in adults first involves double-sided innervation; as training goes on, the impulses are increasingly localized, resp. inhibited. In case of early acquired injuries of the brain, the primitive state is maintained forever, the damaged hemisphere producing a poor inhibition. When the mature cerebrum is injured, some degree of deficient inhibition may result.

In this conception the pathological finds represent an example of "primitivising" or—in Hughling Jackson's term—"dissolution" of the central nervous system.

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Concurrence of Dystrophia Myotonica and Dystrophia Pigmentosa Retinae¹

By

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Modern valuable publications on dystrophia myotonica (*Thomasen, Frövig*) have stimulated the general interest in this disease. Recently we had occasion to observe a case of dystrophia myotonica attended with retinal pigmentary dystrophy ("retinitis pigmentosa"). This combination having not been described before, the case history may be of interest.

First, however, there may be reason to recapitulate certain features concerning both dystrophia myotonica and retinal pigmentary dystrophy, features which are of importance for the present observation.

DYSTROPHIA MYOTONICA

Danish literature contains both casuistic reports on the disease (*Ladekarl* and *Stürup, Hess Thaysen, Pedersen*) and a comprehensive monograph (*Thomasen, 1948*), to which reference may be made. It appears that the clinical picture, in addition to the myotonic dystrophy, localised preferable to masseters and muscles of the forearm, presents also various dystrophic signs and symptoms from epithelial tissues (cataract in 60 to 70 %, alopecia) and endocrine glands (gonadal hypotrophy, and thyroid insuffi-

¹ Read before the Oto-Neuro-Ophthalmological Society, Febr. 18, 1948.

ciency), as well as mental disturbances involving mental retardation. Furthermore, cardiovascular disturbances have been observed (prolongation of the P-Q interval in the electrocardiogram and acrocyanosis), and finally symmetrical degenerative changes in the macula lutea (Verrey, 1947).

Dystrophia myotonica is a hereditary disease with dominant inheritance. It manifests itself chiefly within the age-class of 15 to 20 years, and there is no sex limitation. The prognosis is very poor; after a progressive course the disease will end fatally about the age of 40. The etiology is unknown, and no efficient treatment has been found. Among the myotonic diseases dystrophia myotonica is by far the most frequent one. *Thomasen*, for instance, in the course of 10 years, collected 101 cases of dystrophia myotonica, but only 29 cases of *Thomsen's* disease.

DYSTROPHIA PIGMENTOSA RETINAE

Retinal pigmentary dystrophy has likewise attracted increasing attention within recent years, having more and more frequently been observed to form part of more or less comprehensive neuropsychiatric syndromes with dystrophic features. The term retinal pigmentary dystrophy covers, and is now applied instead of "retinitis pigmentosa", the latter being inadequate, since it is not a question of retinitis, but of abiotrophy.

The clinical picture of retinal pigmentary dystrophy will not be further discussed in this place, the ophthalmological textbooks giving sufficient information. Only it may be emphasised that we have to do here with a hereditary, bilateral, chronic, progressive abiotrophy of the neuro-epithelial elements of the retina, which are replaced by pigmented connective tissue elements. The inheritance is recessive, and the disease manifests itself chiefly within the first decade, more often in males than in females. In addition to the characteristic night blindness we find annular scotomas, gradually developing into concentric visual field constrictions, while the central vision is preserved the

longest. Ophthalmoscopically the waxy optic disk and the extremely contracted retinal vessels, as well as the bone-corpuscle-like pigments are typical, but not pathognomonic, since forms without or with atypical pigments constitute 18 % (*Kjerrumgaard*).

Retinal pigmentary dystrophy forms part of a great variety of syndromes. Thus it is found in association with abiotrophy of the internal ear (*Mygind, Lindenov, Kjerrumgaard*). Furthermore, it is present in *Laurence-Moon-Biedl's* syndrome (together with adiposity, mental deficiency, and polydactylism), in certain forms of idiocy, with or without attending epilepsy (juvenile amaurotic idiocy of the *Spielmeyer-Stock-Vogt* type) (cf. *Sjögren*, 1931), and in various specific abiotrophic heredo-ataxias of the spino-ponto-cerebellar type (*Bogaert, Leuwen, Franceschetti*). The syndrome of heredopathia atactica polyneuritiformis, recently described by *Refsum* (1946), should no doubt be reckoned among the latter. Retinal pigmentary dystrophy may also, but more rarely, indeed, be associated with cataract, nystagmus, growth disturbances of the type seen in endocrine dysfunctions, abnormalities of the bones of the skull, notably a high domed palate (as may also be found in *dystrophia myotonica*). Combination of progressive muscular atrophy and progressive neurolabyrinthine deafness has been observed by *Walsh* (1948) in two brothers, aged 3 and 6 years, respectively.

OWN OBSERVATION

Case History.

The patient is a former journeyman painter, aged 28, (N. P. J.), who now receives disablement benefit. Born 31/7/1920. Within the years 1936-48 he had been admitted altogether 6 times to the Neurological Department of the Kommunehospital (Case 1214/47) for *dystrophia myotonica*. The patient is identical with Case 42 of the series described in *Thomassen's* M.D. thesis.

Genetically the patient belongs to a *dystrophia myotonica* family (Fig. 1), of whose 55 living members 7 have the disease. The parents are not related. The father had presenile cataract (operated on), but not retinal pigmentary dystrophy nor myotony. The patient is a twin, dizygotic. His brother suffers from nocturnal enuresis and incipient cataract, but not myotony. A father's brother's son and daughter both have *dystrophia myotonica*.

Past history: Fracture of the femur at the age of 5 years, but otherwise in good health during childhood. Has been *night blind* as long as he can remember. Between the ages of 10 and 18 steadily increasing difficulty of relaxation of masticatory muscles and muscles of the forearms or hands, which, together with progressive impairment of intellect, compelled him to give up his occupation as a journeyman painter.

The admissions to hospital took place in relation to falls with the bicycle resulting in concussions of the brain, the patient being unable to manage critical traffical situations owing to the failing power of relaxation of the hands. Never cranial fractures, however, (X-ray of skull from 3 aspects 1936-47 showed normal conditions).

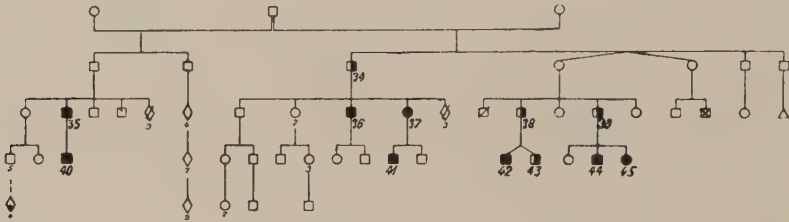


Fig. 1.

Pedigree of family with dystrophia myotonica (from Thomassen).

Case 42 is the case under review with retinal pigmentary dystrophy.

Physical examination: The following stationary features during the past 4 or 5 years was observed: characteristic myotonic facial expression, fronto-parietal alopecia, looks older than his age. Normal build of body. Scanty growth of beard. Mentally infantile, sluggish, and indolent. Voice hollow and toneless.

Neurologically typical myotonic, delayed relaxation, both after voluntary contraction and after direct percussion, of both masseters as well as of muscles of forearms, hands, and shoulder zones, was observed. The myotony was not increased by cooling of the hands in cold water. There was no marked atrophy of the myotonic muscle groups. The remaining neurological examination revealed normal conditions.

Electromyography, 1943, (from the right hand) showed shower-like discharges indicating spontaneous activity at rest, and persistent activity after maximal contraction.

Muscle biopsy, 1948, (from the deltoid muscle) revealed atrophic muscular changes of peripheral muscular origin (Dr. Erna Christensen).

Ophthalmological examinations within the 10-year period showed moderate progressive impairment of the central vision from 5/6 (in 1936) to 6/12 (in 1948), alike in both eyes. Visual fields (5 and 10/300 white and red objects) were normal in 1936, but now (Fig. 2) there is concentric constriction, particularly so of the right eye, and enlarged left blind spot (10/1500 white).

Slit-lamp examination revealed in both eyes slight punctate, posterior, cataractous opacities.

Pupillary conditions normal, in particular no myotonic reaction.

Ophthalmoscopically both eyes presented: slightly yellowish pale waxy optic disks. The vessels, in particular the arteries, universally contracted. Peripherally in the fundus, notably inferiorly, multiple, black, perivascular arranged pigments of different shapes and sizes, yet none of the typical bone-corporuscle shape.

Examination of dark vision (test of distinction) showed considerable impairment (0.00).

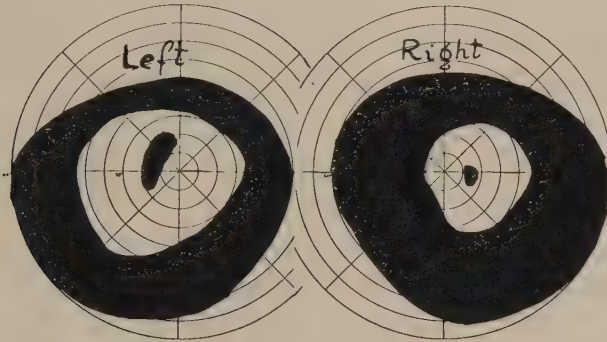


Fig. 2.

Visual fields (white object 10/300 mm.) from patient with concurrent retinal pigmentary dystrophy (presenting constricted visual fields) and dystrophia myotonica.

Cardiovascular system: normal electrocardiogram, though with a low rate (45-60). P-Q interval normal. There was acrocyanosis.

Blood pressure 135/85 in 1938 and 115/70 in 1948 (Hg manometer) .

Otological examination: normal conditions on inspection.

Audiogram showed slight treble deafness suggestive of a light perception lesion. Rotation test showed sluggish labyrinthine reaction in both ears.

Laboratory analysis:

Urine: no albumin, nor blood.

Blood: Wassermann test negative. Sedimentation rate 2 mm. Complete blood analysis: erythrocyte and leucocyte counts normal.

Blood sugar 85 mg^o/. Serum calcium 10.8 mg^o/. Serum phosphorus 3.8 mg^o/. Creatinine 25.5 mg^o/. Creatinine index 109.

Cerebrospinal fluid examined twice: (1) in 1936: 5/3 cells, 1 globulin, 25 albumin (by Bisgaard's method). W.R. negative. (2) in 1947 (shortly after severe head injury): 0/3 cells, 0.1 globulin, 40 albumin (by Bisgaard's method).

The *treatment* has consisted in alternately quinine, vitamin B, and carbon arc light baths.

Epicrisis. A man, aged 28, belonging to a dystrophia myotonica family has since the age of 10 years presented a light, progressive, typically located myotony. There is myotonic facial expression, alopecia, cataract, mental retardation, and acrocyanosis. Has always been night blind. There is bilateral retinal pigmentary dystrophy with progressive visual field constriction and moderate impairment of vision. Examination of the acoustic-vestibular function shows a light perception lesion. Laboratory analyses of blood electrolytes and cerebrospinal fluid, as well as electrocardiogram, show normal conditions.

DISCUSSION

This patient presents a typical dystrophia myotonica localised to the sites of predilection, as well as various other dystrophic signs (alopecia, cataract), mental retardation, and acrocyanosis. Remarkable is the association with massive night blindness, concentric visual field constriction, and bilateral retinal pigmentary dystrophy with typical changes of optic disk and vessels, but less typical pigments. Atypical retinal pigments are, however, more frequent than previously supposed (*Franceschetti, Refsum, Taylor, Kjerrumgaard*) in retinal pigmentary dystrophy. The concurrent lesion of the internal ear of the perception type is suggestive that we have to do with one of the more comprehensive abiotrophic syndromes affecting simultaneously the sensory epithelia of eye and ear, as well as the central nervous system and the muscles. As stated above, our knowledge of these polymorphous syndromes is still being extended. Pathogenetically the diseases are regarded as abiotrophies.

No cases with retinal changes were observed in the previously published large materials of dystrophia myotonica (*Thomassen, Frövig*). This does not preclude, however, that retinal changes may conceal themselves among the cases with cataract. Future clinical investigations into this question may show whether the observation here reported is more than a chance concurrence of two rare dystrophies. The great number of clinical, dystrophic points of resemblance between groups of patients with dystrophia myotonica and retinal pigmentary dystrophy, respectively, suggest that we have to do with a nosological entity so far unnoticed.

SUMMARY

A case is reported of dystrophia myotonica (with cataract, alopecia, etc.), in which there is bilateral, retinal, pigmentary dystrophy as well. Modern literature on both dystrophia myotonica and dystrophia pigmentosa retinae ("retinitis pigmentosa") is briefly reviewed. Finally it is discussed whether the combination observed is a chance concurrence or constitutes a nosological entity so far unnoticed, belonging to the comprehensive syndromes of hereditary abiotrophies affecting chiefly the sensory epithelia of eye and ear, as well as the cerebrospinal system (juvenile amaurotic idiocy, *Laurence-Moon-Biedl's* syndrome, the heredo-ataxias, *Refsum's* disease, and others).

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A Case of Hysterical Paraplegia Cured by Abreaction under Hypnosis

By

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The problems of neurosis and the need of an adequate therapy become increasingly apparent both in general practice and in all kinds of hospital departments, and are possibly felt most acutely by the neurologist. The treatment of neuroses is complicated and time-consuming. Consequently only a few patients can be treated during admission to departments not particularly adapted to the purpose. In the Neurological Department, Aarhus, psychotherapeutic measures have been taken successfully in a minority of neurotic cases presenting rather trivial clinical pictures, such as the case of hysterical paresis reported below.

Case report 3120/46: A cook apprentice, aged 19, was admitted to the Neurological Department, Municipal Hospital, Aarhus, Jan. 3rd, and discharged April 6th, 1946.

History: No familial occurrence of nervous or mental disease. At the age of 9 he had sustained a slight cranial trauma and at the age of 12 a contusion of the left knee. Two months before admission he suddenly developed weakness of both lower limbs, which trembled and sagged at the knees, when he tried standing. The degree of weakness and of gait disturbance varied, so that at times he was able to walk, though with considerable difficulty. For the last year he had had some personal troubles. His master would not acknowledge 8 months' service onboard a state-ferry

as valid apprenticeship. As a result he had to postpone a professional course. Further, he had always wanted to go to sea, but his parents would not allow him to do so. Despite thorough interrogation he was unable to recall any particulars, e.g. the exact time of onset of the disease.

Examination: Height average, body build athletic, harmonic. His intelligence was normal, he was alert, civil, frank, had a charming smile, seemed rather vital, not asthenic, but suggestible and somewhat infantile. e was tense and tremulous, but his attitude towards his tremor was indifferent, and his mood was neutral.

A paresis of both lower extremities was disclosed. The loss of power was "functional " in type, with "antagonistic effort" on examination of knee and foot movements. He showed exaggerated knee jerks, bilateral ankle clonus, absence of the left plantar reflex and hypæsthesia—hypalgesia of the left foot and leg reaching a circular line of demarcation just below the knee. On one occasion a positive Rossolimo sign was elicited on the left, and at the same time there was a questionable Babinski response. He was unable to maintain the erect posture; he would sag at the knees and put his hands to the floor for support. His legs trembled, and on account of the ankle clonus he resembled a crawling step-dancer, when trying to walk. The gait disorder was grotesque and did not vary much. The usual routine examinations, e.g. the spinal fluid and the E.E.G., were normal.

His condition was classified as a hysterical spastic paraplegia. And an interrogation as to possible causal factors was started with, as it turned out, undue optimism. Neither the patient nor his parents nor his working mates knew of any relevant conflict. Hypnotism was then resorted to. The patient was highly suggestible, and the hypnotic sleep was immediately profound. However, a thorough interrogation did not add any new points to his account. A tentative suggestion directed against the paraplegia failed.

The result being so poor, he was subjected to convulsive treatment (3 pentazol convulsions). This was ineffective as far as the disorder of gait was concerned, but transiently the left plantar reflex was elicitable, and the sensory disturbances almost disappeared.

Previously no particular attention had been paid to the sensory disturbances, and the fact that they were sharply delineated corresponding to a small scar just below the left knee had been overlooked. The scar resulted from the above accident at the age of 12. During a hypnotical séance his attention was then concentrated upon that accident. He reported some details, for instance, that he was cycling, when the chain broke. At this stage the past tense was changed into the present tense. And suddenly the patient acted as were he cycling down-hill at great speed. He clung to the handles of the imaginary bicycle for dear life, went pale, his eyes wide open, and suddenly he cried out and threw himself headlong to the ground, where he lay prostrate, first gasping, then stuporous for a few minutes. When awakened he was able to recall only fragments of the events. Under later hypnotic séances it was impossible for him to recall other and later events of a similar character despite repeated association attempts.

However, during a demonstration of other features under hypnosis a clue to his particular problem was offered unexpectedly. On suggestion he became deaf, and in order to demonstrate that fact to the audience the observer clapped his hands. Immediately the patient was seized by a sudden, violent and unexpected fear, and it therefore seemed reasonable to assume that possible pathogenic situations might be connected with loud crashes or explosions.

In March 1946 a series of hypnotic séances were performed during which several pathological anxiety reactions were disclosed—all connected with explosions.

When working as a cook apprentice onboard a state-ferry he witnessed a bombing attack on a nearby German ship. He was

terrified, his consciousness was clouded, and he fell to the ground and could not move for 2 or 3 minutes. Similar reactions followed his witnessing a "Schalburgtage" (Danish Quisling bombing), and again one month before the onset of paresis. On the last occasion some of his class-mates put a small home-made bomb under his chair at the evening school. At the explosion he collapsed in a cataleptic state for some seconds. When, on "coming to", he became aware of his mates laughing at him, he rushed at them, weeping with fury, striking and fighting wildly for some time. It was long before he cooled down. And during the following days he would tremble all over when remembering the event.

All the said episodes were reproduced and re-experienced under hypnosis. When the relevant events were approached with as few specific suggestions as possible, he would, as it were, spontaneously build up and re-enact the situations with so remarkable intensity and in so life-like a way, that the observer had the impression of witnessing the actual incident.

The onset of paresis was eventually fixed at Oct. 30th, 1945. That day he had counted a half-holiday, but because of the illness of a colleague the patient had to work after hours and on his own responsibility. He was under some strain and annoyed at losing a half-holiday, but at the same time he was eager to hold his own. Under hypnosis the patient told about the sequence of events and about a crash which resulted from a waitress's dropping a pile of metal dishes on the stone-floor just behind him. During the séance the patient was observed acting, talking, and working busily. The observer produced a crash, and all of a sudden the patient chilled and started, but immediately and completely, to the astonishment of the observers, pulled himself together brutally crying out: "Damn that old" showing no signs of fear—but at the very moment his legs began trembling violently.

All the said situations were re-lived by and discussed with the patient, and a tentative demonstration of the causal connection

was performed. It was especially emphasized that his having fought and suppressed his fear on the last and fatal occasion had been an essential cause of his gait disturbance.

Thus conditioned he was made to re-experience the fatal situation under hypnosis, and this time an extremely dramatic and extroverted fear reaction was released.

The gait disturbance did not disappear immediately, as had been expected, but two days later he was able to walk normally for short periods, and following continuous treatment, including post-hypnotic relevant suggestions, the gait disturbance disappeared. His various actual problems were fully discussed, and so was the planning of his future, all with the aim of consolidating the therapeutic result through re-education. On discharge he was considered able-bodied. After a year he passed his examination, became a cook, and he has since been doing well and reached his goal, viz. become a cook on a ship.

SUMMARY and COMMENTS

A man of 19 experienced a series of abnormally increased and, under the time of treatment, repressed fear reactions elicited by adequate stimuli. He suddenly developed a persisting hysterical paraplegia, which was resistant to convulsion treatment and direct hypnotic suggestions. Under deep hypnosis he reproduced and re-lived several increasingly pathological fear reactions. All of them occurred in conjunction with explosions, and the paraplegia developed in immediate connection with the last one. The early reactions, obviously not being suppressed, were in the main extroverted. They were characterized by a primitive automatism and uniformity. And the intensity seemed to be increasing. Eventually other features supervened, for instance, in a situation in which his mates made a tiny bomb explode behind him. He was deeply hurt by their scornful laughter. And it seemed reasonable to assume that this violation made him particularly vulnerable and drew his attention to his special weakness. This,

in turn, was possibly the main cause of the change of reaction in the fatal next situation when the paraplegia developed following the crash of some dishes dropped on a stone-floor behind him. He then overcame his fear immediately and did not display his usual picture of terror, cries, wide open eyes, stupor, etc., but, conversely, developed a persistent gait disturbance, which disappeared only after abreaction under controlled though scarcely optimal hypnotic conditions.

This "simple" case history with its almost coarse way of putting the problems seems to show how special emotional reactions may be associated with endopsychic conflicts and violations of the personality, and how, for instance by suppression and repression, pathological psychosomatic symptoms may develop. And the case history shows how brief psychodynamic "analysis" and abreaction can resolve such symptoms.

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Alexia-Agraphia

A Case Report

(acquired reading and writing disabilities, temporary word-blindness of the congenital type)

By

KNUD HERMANN

Most cases of acquired alexia and agraphia appear as part of an aphasia or a Gerstmann's syndrome in sufferings localized to the speech area or parieto-occipitalis, whereas disturbances of the reading and writing functions in cases of slight diffuse cerebral lesions only occur at rare intervals. The following is a report of such a case, which may at the same time tend to the elucidation of congenital word-blindness.

CASE HISTORY

An 11 year old girl without dispositions to nervous diseases in her family, in particular no cases of congenital word-blindness or stuttering. All the members of her family are right-handed.

She is the first of four children. Her birth was a little protracted, but uncomplicated and without asphyxia.

At the age of two she had a—not further diagnosed—high-febrile suffering and later on German measles and chicken-pox. Finally, when she was three years old, symptoms of a heart disease appeared.

Her present suffering began five years ago (1942) with convulsive seizures localized to the left arm. In the course of the two following years she had 5-6 such fits, after which no fit appeared until 17th February 1946, when she was again seized by convulsions localized to the left arm accompanied by mental dimness and possibly hallucinations.

After this last fit word-blindness developed, with disturbances of the reading and, especially, writing functions, but without other aphatic phenomena (see below).

From 15th March to 2nd April 1946 she was admitted to the neurosurgical department of the Rigshospitalet. She proved to be right-handed, and it was confirmed by her parents that she had always been decidedly right-handed.

The objective examination revealed (1) divergent squinting, (2) a very slight paresis of the left arm and leg with preponderance of the left knee-jerk, (3) a mb. cordis mitralis (perhaps congenital).

*Den kloge Hund.
Paa en af de største Bjerger
i Norge, gik en Vinterdag
en gammel Mand.*

D (=D) u (=ü) F P (=P)

Fig. 1.

Normal handwriting and in the last line disfigurement of some letters in the days preceding the convulsive fit.

Electro-encephalography: Slight dysrhythmia over the left and moderate over the right hemisphere.

Ventriculography: A somewhat dilated system without signs of dislocation or focal lesions.

The cerebrospinal fluid: Normal.

During her stay in hospital no convulsive fits were observed, and she felt well when dismissed.

In order to have her alexia and agraphia further elucidated inquiries were made at the school where at that time she frequented the fourth elementary grade. It was stated that she was a clever, particularly intelligent pupil, who with joy went into her schoolwork thoroughly. A tendency to invert the order of letters had never been observed with her, neither in her written work nor in reading. Some of her exercise books were examined, and in checking 805 words a total of 10 errors was found (1.2 % or 1 error per 80 words). All the errors proved to be trivial mis-spellings, but in the days from 8th February to 15th February 1946 (i.e. the 9 days preceding the convulsive fit on 17th February 1946) a slight disfigurement of the writing is observed with uncertainty as to a few letters (see fig. 1).

Her father stated that from 19th February 1946 he had noticed a "sort of word-blindness", as her writing that had been neat till then "degenerated", and she made a great number of errors, just as, when reading, she was inclined to invert the order of the letters. There were no difficulties of speech or trouble in doing sums.

While she was staying in the neurosurgical department an alexia and rather a massive agraphia were established.

The specimens of writing. Of 197 words 37 were mis-spelt (18 % or 1 error per 5.3 words). The corresponding figures before the seizure on 17th February

*Saaet Lar til at sedde et Par Tind
i Daghesthyen. Tak for alle de nye og Ad-
sine. Jeg glæder mig meget til at
du kommer i Mergen*

$\beta (= B) \quad \mathcal{D} (= T) \quad \sim (= x) \quad \mathcal{N} (= n)$

Fig. 2.

were 1.2 % or 1 error per 80 words. Among the 37 mis-spellings there were 14 kinetic reversals (gods for gods,—skure for skruer,—tenge for tegne,—nøgle for nøgle,—skirve for skrive,—re for er, etc.). But besides she was several times on her way to making reversals (Jofes for Josef,—vong for vogn,—talve for tavle, and the like); however, she discovered it in time and made corrections, so that these spontaneously corrected errors have not been included in our statement. Static reversals were not found. Among the remaining 23 spelling mistakes some were quite trivial, while others were due to omissions of single letters and confusions of letters where there is a morphological similarity between the symbols (n for m,—e for i,—r for n). Furthermore the handwriting was small and crabbed with a number of disfigurements (see fig. 2).

Correspondingly, under application of isolated block letters (toy letters) kinetic, but not static reversals were found (BDA for BAD,—and DEU for DUE), but in these cases the errors were at once corrected spontaneously.

The oral spelling likewise showed reversals.

The reading was also rather heavily compromised, as she inverted the order of the letters (vig for giv,—stern for strenge; and Akonkagua was read Ano, An, Anokagua,—Semiramis became Simeramis). To this came a trifling number of other errors (imødekommenhed was read imødekommed, and tror was pronounced tor), but it is possible that these examples can also be explained by the reversal tendency. The reading was slow and hesitating, as a rule correct, but when she spelt her way whisperingly through the words, which

she often had to do, she was heard to make many kinetic reversals. Her conception of what she read was always correct, and she could retell it satisfactorily.

At the aphasia test (Fog & Hermann) no disturbances of the language function were found apart from the alexia and agraphia already mentioned. She perceived the isolated letter symbol without difficulty, and the copying was irreproachable.

Numbers were read correctly, but when writing down numbers above ten she was inclined to invert the order of the digits and the tens, which is easily

Til Jul skal vi spille Julekomedie,
seg skal være en I kulelærer,

Fig. 3.

understandable because in Danish the digits are mentioned before the tens (i.e. 25 is pronounced five and twenty).

With a view to a Gerstmann's syndrome, if any, she was tested for right-left confusion, finger agnosia, and dyscalculi, none of which were present, however:—thus she worked quickly with mental arithmetics (5×5 , $4 + 11$, $13 - 7$, 11×3 , $27 - 3$, and $27 - 11$ were all correct).

No object agnosia or apraxia, no constructive difficulties as to geometrical figures, and finally an intact spatial orientation.

Psychically she seemed to be quite natural; intelligent with clever and quick answers.

After her dismissal the alexia and the agraphia soon bettered, and in the course of June 1946 they had disappeared completely, i.e. four months after these symptoms made themselves felt. She began school again after the summer holidays and managed well again. A specimen of her handwriting from November 1946 is given in Fig. 3, and it shows quite normal morphology of the writing.

COMMENTS

In the present case no exact diagnosis can be made on the basis of the anamnesis or the objective findings. There can be no doubt that there is a diffuse cerebral affection in a right-handed person with its maximum in the right hemisphere (left-sided seizures, and the dysrhythmia most pronounced over the right hemisphere), while no signs of a severe focal lesion are revealed.

In 1938 Kanzer reported a case which in many respects may call the present case to mind: A schoolgirl aged 14 had for two years suffered from generalized convulsive seizures. An encephalogram revealed moderate internal hydrocephalus, but no evidence of a focal lesion. In the last few months she had shown difficulties in spelling, and an analysis of the mistakes among others errors revealed a marked tendency to invert the order of letters both in oral spelling and in writing with the right hand, but they were not present in written products of the left hand. The general intelligence was average for a child of her age, but subnormal in performances requiring visuokinesthetic activity. Some times there occurred aphasic disturbances of an amnesic type, while there was no finger agnosia, no disorientation for left and right, and no difficulty in arithmetic. She had an early disposition to left-handedness, which had been overcome by training. Kanzer is of opinion that the writing disabilities are a result of the diffuse organic disease of the brain, the artificially developed dominance of the left hemisphere produced disintegration and regressive disturbances, which account for the disability in spelling and other disorders reported in this case.

In our case there was no probability that we had before us a masked left-handedness and, consequently, an original dominance of the right hemisphere, as our patient herself and the other members of her family were decidedly right-handed.

In many respects her agraphia might call to mind the one met with in Gerstmann's syndrome. Thus Gerstmann writes about one of his patients: "Es ergeben sich verschiedene paragraphische Entstellungen, perseveratorische Reaktionen, Auslassungen, Umstellungen, Verwechslungen und Verdichtungen der Buchstabenfiguren und Silben, sinnlosen Buchstabenkombinationen usw." And Lange states about one of his patients with Gerstmann's syndrome that when writing figures and words she produced a large number of kinetic reversals, whereas the oral spelling was completely intact. Reading disabilities are also seen in such patients, and the patient just mentioned could read

correctly with the exception of a few instances when she changed the positions of words in sentences.

However, it will be difficult to classify our patient under the Gerstmann cases, as she offers no finger agnosia, right-left confusion, or dyscalculi. And correspondingly it is hardly probable that her agraphia and alexia originate in an affection of the speech area, when not even a slight indication of other expressive and impressive functional disturbances have been established.

If anything, comparison should be made with the congenital word-blindness where we find disturbances of the reading and writing functions without other aphathic or agnostic phenomena, inter alia with frequent kinetic reversals and morphological disturbances of the handwriting (cf. a former work by Hermann & Voldby). In congenital word-blindness there is hardly any organically establishable cerebral affection and at any rate no severe lesion of the speech area or the parieto-occipital area. In this functional disturbance one must reckon with a specific primitivizing of the partial functions serving the reading and writing faculties. On the analogy of this it might be imagined in the case of our patient that through a diffuse cerebral affection her suffering had disturbed these partial functions. But more important than these considerations it seems to me here to ascertain that we have a patient who *acquired* difficulties in reading and writing of the type occurring in congenital word-blindness, which in the unfinished discussion about the proper nature of the latter complaint: either quantitative or qualitative disturbance, must give some countenance to the opinion that the congenital word-blindness is a specific (qualitative) functional disturbance and not simply a merely quantitative variant.

SUMMARY

In the days after a convulsive seizure of the left upper extremity an 11 year old girl develops a massive agraphia and alexia, characterized by a very pronounced tendency to kinetic

reversals. No other aphatic or agnostic disturbances are established. Her difficulties of reading and writing—a functional disturbance of which she has never before shown any symptoms—are so similar to those met with in congenital word-blindness that they may be confused with them. The agraphia and alexia disappear spontaneously and without trace in the course of about four months.

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Arachnoiditis in the Posterior Fossa

An account of 36 cases.

By

HELGE HERTZ

Arachnoiditis, meaning inflammation of the arachnoid membrane, has been, and is a great problem amongst the neurological terms. Under the name of "meningitis serosa" the diffuse form was first described in 1893 by *Quincke*.

Amongst the localized intracranial forms, arachnoiditis of the posterior fossa was first described in 1924 by *Gilbert Horrax*, who reported on 33 cases from Harvey Cushing's department. Horrax divided arachnoiditis into generalized, and localized forms, and primary and secondary forms, the secondary form being secondary to tumours, brain-abscesses, or other localized diseases of the brain. Since then, however, the term arachnoiditis has been the object of discussion.

The neuropathologists have pointed out that the term primary arachnoiditis is illogical, as normally the arachnoid membrane contains no vessels, and therefore cannot be infected primarily. The term arachnoiditis is now generally used for describing a condition of adhesions and cysts in the subarachnoid space, but does not necessarily imply any active inflammation.

An aseptic origin of such a condition has been clearly demonstrated recently by *Arnvig* 1948 in his thesis. By means of a single cisternal injection of a small amount of dead bacteria a progressive arachnoiditis with hydrocephalus was produced in guinea pigs.

A further difficulty in the use of the term arachnoiditis, is the fact that practically all neurological symptoms may be explained by "diffuse arachnoiditis", and owing to this fact, the term has been frequently used where no other diagnosis could be established. Therefore it may be of interest to analyse the symptoms in a series of cases where the diagnosis has been confirmed by operation, and by postoperative observation over a prolonged period.

In our clinic the cases of the cerebello-pontine localization of arachnoiditis have been published by *Hald 1947*, and the cases of chiasmal arachnoiditis by *Knudtzon 1944*.

A description is given below of arachnoiditis localized to the posterior fossa. Excluded are patients with symptoms of a more generalized localization of the disease, but in our opinion the posterior fossa manifestations are part of a generalized disease without generalized symptoms (arachnoiditis in *primis fossae posterioris*).

The material consists of 36 cases of which, with exception of one, arachnoiditis of the posterior fossa was verified by operation, in one case the diagnosis was uncertain.

In 24 of the cases, the diagnosis was verified microscopically, the remaining 11 at operation showed typical macroscopical alterations in the arachnoid membrane. 14 out of 36 patients were female and 19 male. In 29 patients the clinical diagnosis before ventriculography was mid-line tumour, or tumour in the posterior fossa. One case was diagnosed as stenosis of the aqueduct, while six cases were diagnosed as arachnoiditis prior to operation.

An attempt is made at explaining, the origin of the disease in the different age groups of the 36 patients: 4 aetiological groups are used. (1) *Infections of the ear*. (2) *Trauma* (especially in cases of traumatic subarachnoidal hæmorrhage, where blood collects in the posterior fossa when the patient is lying in a supine position). (3) *Syphilis*. (4) A group termed "*toxic*" (postinfectious), meaning that the arachnoidal symptoms develop after a disease accompanied with pyrexia.

In fig. 1 the age groups are correlated with these aetiological groups. Only one patient was 60 years of age, otherwise the age distribution is almost equal in 10-year groups.

Age	No. of cases	Ear-infection	Trauma	"Toxic"	Syphilis
0-10	of 6 cases	0	1	2 ¹	0
10-20	" 7 "	0	2+2	0	0
20-30	" 6 "	0	2+1	0	0
30-40	" 6 "	2 chr. otitis	4	1 ²	1 + WR
40-50	" 4 "	2	(2)	0	1 (WR —)
50-60	" 6 "	3 (1 case of sinusitis)	0	2 ³	0
60-70	" 1 "	1 chr. otitis	0	0	0

¹ pertussis + parotitis. ² tonsillitis. ³ 1 pyrexia, 1 lungabscess.

Fig. 1.

36 cases of arachnoiditis of the posterior fossa.

Aetiologically it may be deduced from fig. 1, that in 3 patients only there is a correlation between the arachnoiditis and ear infections. 2 cases in the third decade, and one in the fourth, had chronic otitis media with secretion from the ear. 4 patients had scars of the tympanic membrane, and one had chronic sinusitis. The material is small, and it is doubtful whether ear-infections are more frequent in these patients than amongst the average population. All patients were examined by an otologist.

7 patients had had a major head injury during the year in which the symptoms of the arachnoiditis developed, and 6 others had sustained head-injuries at an earlier date, while one could not remember receiving any injury, but had a scar on the back of the neck.

The correlation between head-injury and arachnoiditis appears to be closer than that with ear infections, but it may be pointed out that many of these patients develop unsteady gait and vertigo as the first symptoms, and consequently the head-injuries may be secondary.

5 patients had acute infections immediately preceding the onset of the arachnoiditis (parotitis, pertussis, tonsillitis, abscess of the lung, or fever of unknown origin). One case is worthy of

special note: A 32 year old male gave a history of two years' headache, and uncharacteristic vertigo. For some months he had had jerks in both arms, and diplopia. On examination was found papilloedema of 4 diopters, nystagmus, and increased tendon jerks in both lower extremities. Ventriculography showed a marked hydrocephalus. In the back of the neck was found a number of scars after an infection, and the skin was thickened and vascular. At operation was seen an abnormal greyish-red bone marrow, the arachnoid was thickened, and the foramen magendi obstructed. The first days after operation his condition was satisfactory, but later he developed hyperpyrexia, became infected and finally died. This was previous to the introduction of antibiotics. In this case, it seems probable that the arachnoiditis was secondary to a chronic infection from carbuncles. One patient with a microscopically verified arachnoiditis, showed on further investigation a positive Wassermann reaction in the blood and cerebro-spinal fluid, and the arachnoid inflammation may presumably be of syphilitic origin.

Another patient gave a history of syphilis, but the Wassermann reaction had been negative for several years at the onset of the arachnoiditis, and there is probably no aetiological connection between the two diseases in this case.

Less than	1 month	1 case
	1 "	2 cases
	1- 2 months	4 "
	2- 3 "	2 "
	3- 4 "	2 "
	5- 6 "	4 "
	9-10 "	1 case
	11-12 "	3 cases
	1- 2 years	8 "
	4 "	1 case
	5 "	1 "
	over 6 "	7 cases

Fig. 2.

"Duration" of 36 cases of arachnoiditis.

Fig. 2 shows the duration of symptoms before admission to hospital. *Horrax* distinguished between acute cases that had symptoms for less than 3 months and chronic cases. Nine of our cases belong to the acute group. We believe, however, that there is no clear distinction between these groups. There is no clinical distinction, and probably the disease is older than the symptoms. If arachnoiditis is produced experimentally, as by *Arnvig*, the microscopical picture is dominated by leucocytes during the first two months, but in all our cases, even in the "acute" group, the microscopical picture was dominated by lymphocytes. Fig. 3 shows the symptoms the patients complained of on admission.

Headache	24 cases
Vertigo	17 "
Failing vision or flickering of eyes	7 "
Diplopia	5 "
Tinnitus or increasing deafness	5 "
Nausea and vomiting.....	4 "
Pins and needles in or weakness of extrem....	5 "
Unsteady gait	2 "
Fits	3 "
Exophthalmus, stiffness of neck, pyrexia, drowsiness, polyurea, mental retardation, facial palsy and increasing size of head each	1 case

Fig. 3.

Subjective symptoms in 36 cases of arachnoiditis of the posterior fossa.

The symptoms found on examination of the patients after admission to the Neurosurgical Department are shown in fig. 4. They present a kaleidoscopic picture. 4 patients had decreased hearing of one ear, and 3 of both ears, while 2 had sensory disturbances in the trigeminal region, and 6 facial palsy. Considering these facts it is of significance that no patient was completely deaf in one ear, or had absence of caloric reactions of one ear, a fact that is of importance in the differential diagnosis from the acoustic neurinomas.

26 patients had bilateral papilloedema, 3 blurred disc edges only. The correlation between the pressure and the appearance

Cranial nerves:

III, IV and VI:	paresis of abducens	2 cases
	insufficiency of convergence	1 case
	pupillary difference	1 "
V	diminished facial sensation.....	2 cases
VII	facial palsy	6 "
VIII	unilateral diminished hearing.....	4 "
	bilateral " "	3 "
	nystagmus	10 "
<i>Cerebellar symptoms:</i>	Unsteady gait	1 case
	unilateral disco-ordination	1 "
	adiadokokinesia and hypotonia, bilateral	2 cases
<i>"Motor" symptoms:</i>	unilateral Babinski reflex	3 "
	bilateral " "	1 case
	hemiparesis	1 "
	quadriplegia (spastic).....	1 "
	unilateral exaggerated tendon jerks	2 cases
	tremor of hands	1 case

Fig. 4.

Physical signs in 36 cases of arachnoiditis.

of the fundi in 28 cases where the intracranial pressure was measured at ventriculography, are recorded in fig. 5.

Apart from the acute case, which has only blurred disc edges with a pressure of over 600 mm water, the correlation between the frequency of papilloedema and the pressure is good, although it has been possible to find no correlation between the size of the pressure with the degree of papilloedema. This is also a point of significance, as increase of papilloedema does not necessarily imply an increase of intracranial pressure.

Pressure in mm. water	No. of cases	Choked discs	Papilloedema
0-100.....	1	0	0
100-200.....	5	2	1
200-300.....	5		4
300-400.....	4		3
400-500.....	6		6
500-600.....	6		5
over 600.....	1	1	

Fig. 5.

Correlation between ventricular pressure and frequency of papilloedema in 28 cases of arachnoiditis.

In 25 patients the visual fields were investigated by perimeter, the remaining 11 were non co-operative. The visual fields were of interest in 3 cases only, the others were either normal, or in cases of papilloedema showed an increased blind spot. 2 of the patients with abnormal fields had a unilateral lower nasal quadrant hemianopia, while the third had a nasal hemianopia of the left eye, and only hand movements remained in the lower nasal part of the right field.



Fig. 6.

Visual fields in a case of arachnoiditis of the posterior fossa.

Two reasons may be considered as an explanation of these abnormal fields. (1) The field defect may have been produced by local pressure on the chiasma of an increased third ventricle, as described by *E. B. C. Hughes*, or (2) There may be arachnoiditis also of the optic chiasma.

The 3 cases mentioned above showed a dilated third ventricle on the ventriculograms, but nevertheless the latter explanation seems to be the most probable, as the typical field defect described by *Hughes* consisted of a bi-temporal hemianopia, while 2 of our cases had a unilateral nasal hemianopia, and the third an advanced, homonymous hemianopia. Furthermore, the majority of the cases showed a comparable increase of the third ventricle without field defects.

In 35 patients a routine x-ray examination was carried out, 18 presented signs of increased intracranial pressure: increased impressions, or burst sutures. A small, or vaguely outlined dorsum of the sella was found in 9 sets of x-rays, and only 3 posterior fossae were found bulging. 6 sets of x-rays were normal. These were adult patients.

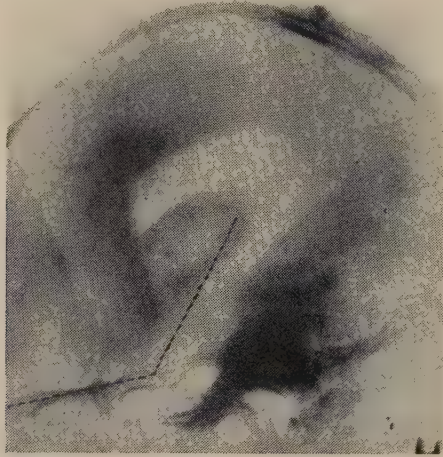


Fig. 7.

Side-view of ventriculogram from a case of arachnoiditis of the posterior fossa. The lines of Lutz and Wilson are indicated in the picture.

(For explanation see text.)

The duration of the history does not appear significant for the development of x-ray changes.

From a clinical point of view, it may be seen that in 50 per cent of these cases a simple x-ray of the skull gives a diagnosis of increased intracranial pressure.

29 of 35 ventriculograms gave the necessary diagnostic information: air in the fourth ventricle, dilatation of the system including the aqueduct, clear filling of the rostral part of the third ventricle showed that the block was in the posterior fossa.

In 4 cases the rostral part of the third ventricle was inadequately filled, and no air was seen in the aqueduct or the posterior fossa. In these cases the clinical symptoms indicated a posterior fossa lesion.

As it is of great importance to distinguish pre-operatively between infratentorial tumours, and simple aqueduct stenosis, *Lutz and Wilson 1946* have recently devised a technique to discriminate these conditions from ventriculograms. A line is drawn along the lesser wing of the sphenoid, and a second from the anterior clinoid process to the suprapineal recess. In normal ventriculograms and in cases of aqueduct stenosis these lines will meet at an angle of 150° , but in cases of infratentorial tumour the angle will be diminished.

This method has been applied to 4 sets of ventriculograms, where difficulties have arisen pre-operatively in diagnosing the level of the block.

In one case it was impossible to use the method as the rostral part of the third ventricle was inadequately filled, and the suprapineal recess could not be clearly visualized. In the other 3 cases the angle measured between 150 and 155° .

Therefore the method in our opinion does not solve the important problem of distinguishing between the supratentorial stenosis of the aqueduct and a infratentorial blocking of the fourth ventricle, which is due to arachnoiditis and not to a tumour.

Two ventriculograms are of special note. One case was a 15

Dilatation of ventricles	Slight	Medium	Severe
Pressure in mm water	280	500	400
	100	470	500
	300	530	240
	80	430	140
		450	700
Average 190 mm		500	260
		500	150
		500	450
		340	230
		500	340
		400	580
		Average 465 mm	500
			Average 374 mm

Fig. 8.

Correlation between ventricular pressure and degree of ventricular dilatation.

year old boy, who had a typical history of eighteen months' duration of increased intracranial pressure. The ventriculograms showed marked dilatation of the ventricle, and the air stopped in the middle of the aqueduct. A diagnosis of aqueduct stenosis was made, and it was intended to perform a ventriculocisternotomy according to *Torkilsen*. On operation it was found that the whole surface of the posterior fossa was covered with bony prominences, it was completely deformed, and the bone abnormally thick. A posterior fossa exploration was now carried out, and a typical arachnoiditis encountered.

Ventricular fluids	Lumbar fluids
25 normal	
4/3-5-50	
8/3-7-40	
	7 normal
	0/3- 1- 7
	1/3- 1- 10
	31/3-20-200
3/3-0- 9	0/3-19-200
2/3-0-10	2/3-30-400

Fig. 9.
Cerebrospinal fluids.

The other case was a 35 year old female, who had a history of 1 year's uncharacteristic headache. For 4 weeks she had had blackouts, vertigo, and pins and needles of the ulnar fingers of the left hand: On admission she had a bilateral papilloedema of 4 diopters, but showed no other neurological signs. On the diagnosis of mid-line tumour a ventriculography was performed. The intraventricular pressure was 200-280 mm, but the films showed a normal ventricular system. A bilateral percutaneous arteriography showed normal vessels, and she was kept under observation for 4 weeks. As the papilloedema increased a ventricular refill was performed. This also showed normal films, except a slight dilatation of the third ventricle, and no air-filling of the

fourth ventricle.—A posterior fossa exploration was then performed, a diffuse arachnoiditis was found, and after decompression the papilloedema gradually subsided.

In all other cases the ventricles were dilated. In the cases where the pressure was measured at the time of ventriculography the degree of dilatation is compared with the intraventricular pressure (fig. 8).

In 4 patients with slight ventricular dilatation the average pressure was 190 mm, in 11 with middle dilatation, 466 mm, while in 12 with severe dilatation it was only 374 mm.

Infection	2 cases
"Block" symptoms	3 " + 1 four days after discharge
Hyperpyrexia	3 "

Fig. 10.

Cause of death in 9 cases of arachnoiditis.

This may be explained by the fact that in cases with so severe dilatation the brain tissue is so atrophic that the high pressure cannot be maintained.

In none of the cases a spontaneous ventricular rupture with subtentorial cyst formation (*Pennybacker and Russell, 1943*) was observed as a cause of spontaneous arrest of increasing intracranial pressure.

In 29 cases the ventricular fluid was investigated. One showed globlin of 1, albumin 10 (Bisgaard Method: normal limits: 1 globlin, 10 albumin). Only 2 ventricular fluids proved abnormal. (1) 4/3 cells, 4-5 globlin, 50 albumin. (2) 8/3 cells, 4 globlin, 40 albumin.

12 patients were lumbar-punctured. 3 only showed significant pathological fluids: (1) 31/3 cells, 19-20 globlin, 190-200 albumin. (2) 0/3, 19, 190-200. (3) 2/3, 30, 350-400. In these 3 cases with grossly abnormal spinal fluid the ventricular fluids were within normal limits, which proves that even in cases with marked arachnoid reactions in the posterior fossa the ventricles may show no sign of inflammatory reaction.

In 2 cases electroencephalography showed diffuse dysrhythmic alterations. Both patients were between 20 and 40 years of age, both had a ventricular pressure of 320-280 mm, and a history of about 1 year's duration. One of these patients had a marked ventricular dilatation and the electroencephalogram showed diffuse slow waves, probably as a result of the high pressure, and a certain amount of cerebral oedema.

In the other case the ventricular system was completely normal on the ventriculogram, but electroencephalography showed marked phase reversals over the left pre- and postcentral region, indicating a process localized in this area. At operation a typical arachnoiditis was found in the posterior fossa, and no signs of arachnoiditis in the supratentorial burr holes.

It may therefore be assumed that the disturbances in the brain circulation produced by moderate pressures are sufficient to give focal electrical disturbances and probably convulsions.

OPERATIVE TECHNIQUE

A bilateral cerebellar approach through the usual horseshoe incision was used, with the exception of a number of children, where a mid-line incision was used. A bony decompression was made, and the dura opened with a curved incision. Arachnoid cysts were opened, and pieces of the arachnoid taken for sections. The dura was left open, and attached to the bone together with the muscles. (After the method of Penfield.) The subcutaneous layer and skin were sutured with silk. Drainage was used in some cases.

In 14 patients anatomical deformities of the bone were encountered at operation. The median ridge was deep, and the posterior fossa flat. It is thought that this deformity may have a certain significance for the development of block symptoms.

8 patients died following operation, 2 of meningeal symptoms, before the introduction of chemotherapy, 3 others from acute block symptoms, which were not relieved by ventricular puncture, and 3 from hyperpyrexia, with no sign of infection. One patient

was discharged in a satisfactory condition 3 weeks after operation but suddenly died from an unknown reason 4 days after discharge, probably from an acute block. These figures show a direct mortality of 25 per cent.

Duration of post-operative observation	Cured	Improved	Unchanged	Dead
0- 1 year	1	1		9
1- 2 years	1			3
2- 3 "	2			1
3- 4 "	1	2	1	2
4- 5 "	1	2	2	
7- 8 "	3			
8- 9 "	2			
10-11 "	1			
11-12 "	1			
total	13	5	3	15

Fig. 11.

Prognosis of 36 cases of arachnoiditis of the posterior fossa.

13 patients were seen, or reports received from their doctors, and they are completely well after operation (fig. 11), free from any subjective symptoms, fit for work, and without abnormal neurological signs. 5 patients are improved, one has papilloedema 6 months after operation, 2 are still suffering from vertigo 3 years after operation. One is almost blind owing to secondary optic atrophy, but otherwise without abnormal neurological signs, and 2 patients are suffering from chronic headaches after 4 years. 3 are unchanged or deteriorated after operation. The patient previously mentioned, who was found to be suffering from cerebral syphilis, has become increasingly demented since operation. A patient operated on at the age of 61, remains unchanged 4 years after operation, and one, who had been well for 4 years post operation, developed symptoms of basal fluid block.

6 patients have later died, 3 in the second year, 1 in the third year, and 2 in the fourth year. 3 of the patients appear to have deteriorated gradually, while 3 others have died from various diseases which may or may not be related to the arachnoiditis.

In conclusion it may be stated that 50 per cent of the patients were improved or cured after decompression, 25 per cent died shortly after operation, and the remaining 25 per cent either died later, or remained completely unchanged.

Probably the arachnoid reaction is either mainly limited to the posterior fossa cisterns, in which case the re-opening of these prevents the symptoms from progressing, or the arachnoiditis has at the time of operation already interfered with the absorption mechanisms of the c.s.f. and therefore the decompression proves ineffective.

13 patients cured	7 had X-ray treatment
9 " unchanged or dead..	3 " " " "

Fig. 12.

X-ray treatment in 22 cases of arachnoiditis.

Approximately half of the cases had x-ray treatment to support the effect of the operation (2000 r. in 2 side fields, and 1 neck field a single dose of 200 r.).

Of the 13 patients cured 7 were given x-ray treatment. In the group of the 9 patients who either died or at a later date were unchanged after operation, 3 had had x-ray treatment. However, the numbers are too small to draw conclusions as to the effect of x-ray treatment in this disease.

The microscopical sections showed the typical picture of chronic infection with immigration of lymphocytes.

Fig. 13 shows:

(a) Section of the arachnoid membrane in a case believed to be of traumatic origin.

(b) Section of the arachnoid membrane of a case proved to be syphilitic.

It appears that the reaction of the arachnoid membrane, irrespective of the cause of irritation, presents an almost identical microscopical picture, which shows that the arachnoiditis is only a form of reaction of the arachnoid membrane. That no signs of infection is present in these cases is further confirmed by the fact

that only in 4 of 32 cases out of this material the blood sedimentation rate was above normal limits, and also leucocyte-counts were normal in the cases where this investigation was carried out.

Summing up the results of this investigation it might be stated that (1) arachnoiditis of the posterior fossa is not a frequent disease since the 37 cases described correspond to over 2000

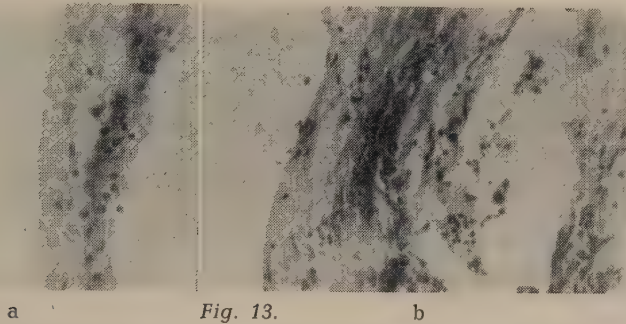


Fig. 13.
Microscopical sections of arachnoiditis: (a) of traumatic origin.
(b) of syphilitic origin.

verified intracranial tumours. (2) The history is either one of slowly progressing disease or one of an attack followed by a gradual improvement. Head-injuries are frequent in the history. (3) The complaints of these patients are usually vague and general. The diagnosis should therefore be based on the physical signs: (a) signs of a surface lesion in the posterior fossa, (b) signs of increased intracranial pressure. The cerebrospinal fluid is normal in over 50 per cent of the cases.

Operative treatment is indicated in cases with signs of increased intracranial pressure.

SUMMARY

The use of the term arachnoiditis is discussed. The posterior fossa localization is part of a generalized condition. Our material consists of 36 cases, 35 of them being operatively verified. The diagnosis is discussed. The cases are aetiologically grouped, only trauma seems a relevant cause (7 cases). One case was syphilitic.

9 cases had symptoms for less than three months, but even those are thought to be of longer duration. Headache and vertigo are the symptoms in 24 and 17 cases. Cranial nerve palsies distinguish arachnoiditis from cerebellar tumours, and presence of caloric reaction distinguishes the condition from acoustic neurinoma. Papilloedema in relation to intracranial pressure is discussed. Three cases with visual field disturbances are described. 18 cases showed signs of increased intracranial pressure on x-ray examination. The ventriculograms are discussed in 4 doubtful cases. Cerebrospinal fluid examination: 3 out of 29 ventricular fluids were abnormal, and 5 out of 12 lumbar fluids. Operation is discussed and the causes of 8 operative deaths. Prognosis is discussed, 18 are cured or considerably improved, 18 later died or are unchanged. The value of x-ray treatment seems doubtful. Finally the microscopical picture is discussed in relation to the origin of the condition.

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Kidney Function in Essential Hypertension before and after Sympatectomy a.m. Peet

By

TAGE HILDEN

The modern tests (inulin clearance, diodrast-Tm, and diodrast clearance) make it possible to determine the various functions of the kidney separately, and a number of results of those tests in patients suffering from essential hypertension have already been published (3, 5, 6).

In brief, the following results have been obtained:

A great number of hypertensives show values ranging within the normal limits, while in the more severe cases a certain reduction of the three tests will occur. As a rule the depression of the renal blood flow (diodrast clearance) is more pronounced than that of the glomerular filtration rate (inulin clearance). The filtration fraction $\left(\frac{\text{inulin clearance}}{\text{diodrast clearance}} \right)$ consequently will be increased. The tubular function (measured by the diodrast-Tm) will show a reduction which is usually more pronounced than the reduction of the inulin clearance, but less pronounced than that of the diodrast clearance.

Several authors have been interested in the changes that appear in the kidney function after sympatectomy in patients with essential hypertension.

TABLE
Data for 20 cases of essential

No.	Sex	Age	Blood Pressure	Retinal Changes Keith & Wagener I - IV	Result of the operation		
					Clinical	Retinal	Blood Pressure
5626	M	54	155-130/ 90- 80	I	improved	unchanged	unchanged
5637	M	33	180-135/ 70- 60	I	improved	unchanged	unchanged
5697	M	54	260-180/140-110	I	aggravated	unchanged	lowered
5362	F	46	270-195/130-100	I	improved	improved	lowered
5346	F	46	145-110/115- 95	I	unchanged	aggravated	raised
5851	F	40	225-180/130-110	II	improved	unchanged	unchanged
5219	M	41	240-180/150-120	II	improved	unchanged	lowered
5693	F	51	300-240/165-140	II	unchanged	unchanged	unchanged
5378	F	45	210-195/130-135	II	improved	unchanged	lowered
5666	M	57	240-230/150-140	II	unchanged	unchanged	unchanged
5756	F	52	240-190/135-130	II	no follow-up study		
5713	F	57	260-180/160-120	II			
5137	M	37	255-210/165-130	III	unchanged	unchanged	unchanged
5371	M	53	215-190/140-125	III	improved	improved	lowered
5373	F	44	155-145/ 90- 90	III	improved	?	unchanged
5187	F	47	265-260/170-170	IV	dead	—	—
5182	M	43	220-210/140-140	IV	dead	—	—
5778	F	42	230-170/140-120	IV	improved	improved	lowered
5193	M	52	220-215/135-120	IV	dead	—	—
5424	F	50	260-220/185-160	IV	dead	—	—

Adams, Alving, Sandiford, Grimson & Scott (1) have discovered no significant changes in the kidney functions (inulin clearance, diodrast-Tm, and diodrast clearance) after sympatectomy a.m. Peet.

Foa, Woods, Peet & Foa (4), using a not very satisfactory technique, have examined the kidney function in 15 patients before and 5-12 months after operation a.m. Peet. They found little if any change in diocrast clearance, while inulin clearance

hypertension operated on a.m. Peet.

Urea clearance			Diodrast clearance			U/D ratio		
Before operation	10 days after	12-18 months after	Before operation	10 days after	12-18 months after	Before operation	10 days after	12-18 months after
82	68	77	776	704	615	10.5	9.7	12.5
80	51	77	750	517	708	10.7	9.9	10.8
64	63	60	533	604	497	12.0	10.4	12.1
82	72	68	657	662	524	12.5	10.9	13.1
76	86	69	598	739	490	12.7	11.7	14.1
36	29		359	367		10.0	7.9	
74	82	61	580	607	377	12.8	13.5	16.2
92	70		620	602		14.8	11.6	
55	70		349	578		15.7	12.2	
52		51	330		316	15.8		16.1
55	57		340	476		15.9	12.0	
48	50		277	372		17.3	13.4	
84	85	59	538	557	495	15.6	15.2	11.9
53	55	54	325	480	348	16.3	11.5	15.5
74	47		406	356		18.5	13.2	
46	45		245	340		18.7	13.2	
47	44		229	299		20.5	14.7	
79	64	57	329	392	263	24.0	16.3	21.6
41	42		150	210		27.3	20.0	
23	18		77	75		29.4	24.0	

showed varying results; the filtration fraction was increased in 8 cases, decreased in 3, and unchanged in 4. Diodrast-Tm was on the whole unchanged.

Talbott, Castleman, Reginald, Smithwick, Melville & Pecora (8) have determined the kidney function in 24 patients suffering from essential hypertension after sympatectomy a.m. Smithwick. Kidney function was determined before the operation and in 18 cases also two weeks later, and in 15 cases 4-15 months later.

They have found inulin clearance to be decreased shortly after the operation, while later on values are almost as before the operation. On the other hand diodrast clearance does not change shortly after the operation, but later values a little lower than before will be found. The filtration fraction will consequently have decreased shortly after the operation. The authors maintain that some months later the filtration fraction is as before the operation, but the figures seem to point to a slight increase compared with preoperative values, this being a direct consequence of the mentioned changes in filtration rate and renal blood flow. Diodrast-Tm has only been carried out in few cases, and the authors point out that they dare not draw any conclusions from this.

TABLE II.

Mean values for 19 cases examined before operation and 10 days after and for 10 cases examined before operation and 12-18 months after.

		Urea clearance	Diodrast clearance	U/D ratio
19 ptt.	{ Before operation	63	429	16.6
	{ 10 days after	58	470	13.2
10 ptt.	{ Before operation	73	541	14.3
	{ 12-18 months after ..	63	463	14.4

OWN INVESTIGATION

Urea clearance and diodrast clearance have been determined in 20 cases of essential hypertension operated a.m. Peet. In all the cases determinations were made before the operation—in 19 cases 10 days afterwards, and in 10 cases 12-18 months after the operation. As to the technique and the chemical analyses reference must be made to previous publication (6).

The relation between the two tests is expressed as U/D ratio,

$$\frac{\text{urea clearance}}{\text{diodrast clearance}} \cdot 100.$$

The normal values of the tests, according to the author's earlier publication, are as follows:

	mean	2.8 x mean error
Urea clearance	74	57-91
Diodrast clearance	613	470-755
U/D ratio	12.1	9.3-14.9

In Table I is given the data of the individual patients. In Table II the mean values of all the cases examined are given.

DISCUSSION

As inulin was not available at the time of the present investigations, urea clearance was used as a measure of the glomerular filtration rate. Although not quantitatively identical with the filtration rate, the urea clearance varies with the changes in the glomerular filtration rate. Diodrast clearance has been taken as a measure of the renal plasma flow. That this may be relied on also when one has to do with patients suffering from essential hypertension seems evident from determinations of the self-depression limit, which is not displaced downwards in patients suffering from essential hypertension (7), and more convincingly from determinations made through catheterisation of the renal vein, which shows the extraction of diodrast to be normal in patients suffering from essential hypertension (2). Diodrast clearance consequently is equal to about 90 % of the renal plasma flow. In a few patients with severely depressed kidney function the extraction of diodrast was found to be subnormal. In the present work this may have been the case in pt. no. 5193 and no. 5424. In these patients diodrast clearance may be somewhat lower than the real renal plasma flow.

Consequently the U/D ratio $\left(\frac{\text{urea clearance}}{\text{diodrast clearance}} \cdot 100 \right)$ —according to what have been said before—must be fundamentally equal to the filtration fraction $\left(\frac{\text{inulin clearance}}{\text{diodrast clearance}} \right)$.

From the above-mentioned results (Table I and Table II) it appears that ten days after the operation urea clearance is unchanged or perhaps a little lower, while diodrast clearance as a

rule is a little higher, the U/D ratio consequently being decreased.

As the blood pressure at that time always shows lower values than before the operation an unchanged or slightly increased diodrast clearance will signify that a considerable dilatation of the renal arterioles (vas afferens and vas efferens) must have taken place. As the U/D ratio has decreased it may be concluded that vas efferens has been dilated to a relatively greater extent than vas afferens.

At the follow-up examinations 12-18 months later the urea clearance as well as the diodrast clearance will be found to be a little lower than before the operation, while the U/D ratio is on the whole unchanged. This shows that the renal impairment caused by the increased blood pressure has continued in spite of the sympatectomy. Whether the renal lesion would have progressed more rapidly without the operation it is impossible to say.

From Table I it will be seen that the clinical results of the operation as well as the course of the blood pressure do not depend on any special change in the kidney function, and it must be especially stressed that no parallelism exists between a permanent fall in the blood pressure and an increased renal plasma flow or reduced U/D ratio.

Contrary to theories prevalent in the late thirties one cannot to-day consider a decreased renal plasma flow to be the primary factor in the pathogenesis of essential hypertension. Nor are changes in renal blood flow, as appears from the investigations presented here, determinative of the results of a sympatectomy in patients with essential hypertension.

SUMMARY

I. Determinations of urea clearance and diodrast clearance in patients suffering from essential hypertension have been carried out before, 10 days after, and 12-18 months after sympatectomy a.m. Peet.

II. 10 days after the operation urea clearance is on the whole unchanged, while diodrast clearance is a little increased.

III. 12-18 months later urea clearance as well as diodrast clearance are somewhat decreased.

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Some unusual Cases of Post-Traumatic Headache

By

HARVEY JACKSON

F. R. C. S. Eng.

As an indication of intracranial pathology headache is, perhaps, the most common feature; and, following the receipt of a head injury, it is almost a daily problem of the neurosurgeon. Well aware as we are of the various types of headache, the hypertensive, hypotensive, meningitic and psychogenic, etc., we continue to meet cases causing difficulties in diagnosis. Recent experiences afforded by the war have brought to notice cases of headache the features of which are not common-place: it is to some of these that reference is considered worthwhile.

Subsequent to penetrating injuries, the intervention of headache ever leads to the suspicion that a cerebral abscess may have developed, yet the diagnosis can prove perplexing. One may feel that no longer should dealing with a cerebral abscess prove an adventure, for with the appropriate use of penicillin rather are we led to anticipate the prospect of a satisfactory outcome. Nevertheless anatomical and physiological considerations call for a degree of temerity in the contemplation of radical methods of treatment.

Case No. 1. A man of 22 years of age received a bullet wound in the left temporal region. He recollects the impact and records that he continued walking for about 200 kilometres before collapsing. Whilst there occurred no abrupt weakness in either right upper or lower limb, he was rendered totally aphasic. Early excision of the surface wound with closure resulted in primary union. Some eight months later he suffered his first epileptiform attack following which he became subject to attacks with intervals between them

of two to four weeks. Initially the attacks exhibited Jacksonian characteristics succeeded by unconsciousness, but latterly loss of consciousness had not been a feature. Throughout neither tongue-biting nor urinary incontinence occurred.

Two years later, owing to the onset of headache—a sensation that there was something unusual present behind his left eye—he was detained in hospital for observation. At this juncture there presented a mildly paretic state of the upper and lower limbs on the right side. However, early and continued improvement took place in that the headache lessened in intensity, no fits

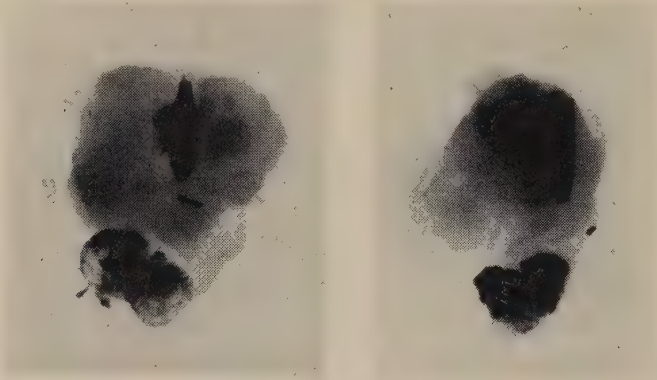


Fig. 1. Case No. 1.

Radiographs of the excised abscess together with the foreign body.

occurred, and the paresis so improved that he was permitted to leave hospital. He resumed light work at once. Regular dosage of phenobarbitone in a half-grain three times a day was maintained. After only a fortnight's activity as a farm hand he was subjected to a series of five convulsive attacks. Following a moderate increase of sedation by a supplementary half-grain of phenobarbitone at night, he suffered but one major convulsion during the next four months. Meanwhile, he resumed activity on the farm continuing in employment for sixteen months, subject to an occasional headache of variable intensity, but not incapacitating. At times he found some difficulty in speech when, whilst knowing what he wished to say, he found enunciation impossible.

Three years and nine months from the time of injury he was re-admitted to hospital in a semi-comatose state subsequent to an epileptiform attack. Lumbar puncture gave no indication of increased pressure and the C.S.F. contained 25 mgm. per cent of total protein, 680 mgm. per cent of chlorides, and no cells.

Encephalographic examination was now deemed essential despite the normal cerebro-spinal fluid. The ventricular system exhibited a moderate generalised dilatation as one would anticipate as compensatory for tissue damage, but the body of the left lateral ventricle was flattened and displaced towards the right. The existence of a bullet in the proximity was no explanation

for the displacement; indeed there appeared to be quite a gap between the foreign body and the ventricle, as against the more likely traction of the ventricle from scarring. Thus the existence of an abscess became obvious.

Lying as the bullet was, directly subjacent to the motor cortex, the risks of operative intervention demanded very serious thought. The attentions of the patient and his wife were drawn to probable as well as possible consequences of surgical intervention with the result that operation was refused. In a matter of six weeks his general condition had deteriorated and persistent clonic movements appeared in the right face, but the patient was still reluctant to submit to surgical treatment. Headache now developing an increasing severity, occasional vomiting and deterioration of memory taking place, finally the patient returned to hospital desirous of early relief, yet fully aware of the attendant risks. By now the hemiparesis had developed considerably.

Following aspirations of pus with the introduction of penicillin into the abscess cavity, the general condition of the patient was observed carefully pending restoration to a state fit for excision of the abscess. Thorotrast, of course, had been injected into the abscess, in accordance with presentday technique, in definition of the size and site of the lesion. Post-operatively the patient was completely aphasic and hemiplegic but an early return of function appeared in the lower limb and the speech. At the present time the patient is making good progress, and the prospect of a useful existence seems assured.

The difficulties in dealing with a case of this sort will be only too apparent to a neurosurgeon of experience. Drastic measures alone offer any prospect of recovery though attended by serious implications. A fatal termination is a useless alternative!

Localised headache sometimes proves to be an entity arising from head injury. The continuous nature and persistent pain in a particular area is important in recognition of its origin. One may infer that in a case complaining in this manner a lesion of restricted extent is responsible. Indeed the most likely pathological explanation is that of a subdural collection of fluid—a Cystic Hygroma or Hydroma. Usually evacuation of the fluid is an entirely satisfactory treatment. That this is not invariably the causative factor is only too well appreciated. As unusual as intriguing is the case to which one now refers.

Case No. 2. In 1941 a fellow of 29 years of age was wounded in the right parieto-occipital region, sustaining a compound fracture. Meningitis superimposed on the injury led to a prolonged period of recovery. Only two months

after the wounding fits of a Jacksonian nature commenced, to recur every four or five weeks. Subsequent to the attacks, he was inclined to headache which lasted up to 48 hours.

He was a healthy looking fellow of stocky type. Deafness in both ears appeared shortly after injury and gradually increased. As no other local cause for his deafness could be found, it was assumed to be one of those cases of progressive deafness of concussive origin. In the right parieto-occipital region was a depressed scar about 2 cm. in length. Clinically, clear evidence of extensive parietal cortical damage existed in cortical sensory depression

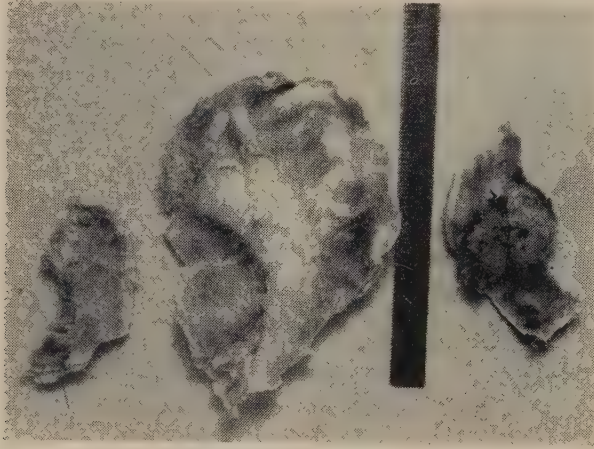


Fig. 2. Case No. 2.
Granulomata of Dura.

involving both upper and lower limbs—astereognosis in the hand, loss of two-point discrimination and spatial orientation in the arm and leg. He showed considerable emotional disturbance, being very disturbed by the sympathetic attention of work-mates and others who attempted to aid him in any way. The main complaint was of headache, localised in distribution with some accuracy, in front of the wound and lower down.

The cerebro-spinal fluid showed a total protein content of 30 mgm. per cent, chlorides 710 mgm. per cent, and no cells. Blood Wassermann reaction was negative. The electro-encephalogram gave an abnormal record consistent with Epilepsy. No focus could be determined.

Encephalography showed a slight dilatation of the right lateral ventricle but no other deviation or distortion. A piece of bone was buried in the cortex beneath the wound described above.

Such was persistence of the headache that operation was suggested and accepted willingly by the patient as he was rather distressed by it.

An osteoplastic cranioplasty was performed at the beginning of 1943 at which a most uncommon granulomatous state of the dura was encountered.

Three patches of gross thickening of that membrane were found and these were excised, the resultant defects being closed by the insertion of fascial grafts. He made a fairly rapid recovery without incident, and was well enough to resume work three months from the time of operation. Naturally his sensory defect persists and this proves troublesome. Nevertheless, he was able to return to work as a carpenter. He is still on a regular dosage of phenobarbitone—this has given him much relief and his attacks have not reached a state of unconsciousness since operation.

What is the mechanism of "Headache"? Many indications lead to the conclusion of its origin within the vascular channels. First of all there is the clinical evidence arising out of the administration of such chemical substances as adrenalin, histamine, nitrites and ergotamine; there is the commonly elicited fact of the extreme tenderness of meningeal vessels when touched during intracranial operations under local analgesia; also there are the disturbances of vascular hypotension and the existence of the condition known as "Temporal Arteritis" wherein the relief of the pain is attained by resection of a portion of the vessel so affected. However, any direct observation of a vascular abnormality whence removal of the fault affords complete relief is not commonplace, so that the case now reported proves of unusual interest.

Case No. 3. A man of 26 years of age was wounded by a shell fragment, receiving a penetrating injury of the right frontal region resulting in an extensive bony defect. Early operative intervention met with healing by primary union. So satisfactory was the post-traumatic recovery that reconstruction of the cranium was undertaken by the writer eight months later. An uneventful convalescence was followed by apparently complete recovery. All went well with the result that the man resumed a normal existence. Some eighteen months later, however, he contracted an influenzal infection for which he was detained in bed. During the course of this illness headache intervened and gradually increased to such an intensity as to lead to absolute incapacitation. It was in this condition that he was re-admitted to hospital. A small metallic foreign body was known to lie in the right temporal region but this had been present from the start; moreover it had apparently remained undisturbed, therefore it was not paid particular attention. Lumbar puncture did not reveal any pressure disturbance, and the C.S.F. contained protein in normal concentration, without cellular elements.

Ventriculographic examination was decided upon. This revealed a very moderate dilatation of the whole ventricular system and a traction-distortion of the right anterior horn in the direction of the foreign body. The interpretation of these findings was of adhesion of the cortex to the dura mater with cicatrization drawing out the horn of the ventricle.

Exploration was carried out with the intention of freeing adhesions and appropriate treatment of the cerebral scar. On reflecting the dura this was found to be adherent on its deep surface in the region of the pterion. Circumvention of this attachment revealed its association with the foreign body. The foreign body consisted of a piece of steel twisted in spiral fashion around which a cortical artery was intimately entwined. Just how this extraordinary apposition of foreign body and blood vessel came about seemed difficult of explanation, but one concluded that arterial pulsation had induced a rotatory movement in the metal to coil the artery around itself. The intervening part of the artery was excised together with the piece of metal, then the wound was closed. Instantaneous relief resulted and no return of pain has occurred to date, a matter of seven months since the operation.

A detail for conjecture is found in the strange interval between the receipt of injury and the onset of the disabling headache. One can but suppose that mobility in the foreign body could be responsible, and this brought about by pulsation within the brain until such time as the piece of metal negotiated the blood vessel.

Delay in the onset of symptoms from the injury subjected to early operation always proves difficult of explanation and the longer the interval, in the absence of sepsis, the more inexplicable becomes the underlying cause. Well does the writer remember a man who reappeared after twenty years. Relief was sought on account of headache and a deteriorating memory. Undoubtedly exploration was called for and this was justly awarded by the presence of a dermoid tumour which must have arisen from a small scalp inclusion at the time of injury.

The author has excised two cerebral abscesses in patients who were admitted to hospital twenty years after being wounded.

The next case to which reference is to be made bears quite different qualities although it appeared as another "post-traumatic headache".

Not infrequently during the interrogation of a patient enquiry as to the nature of a headache is met by the comment that the

complaint "is not really a headache, but a pain in the head". This may usually be taken to infer that the pain is likely to be of other than intracranial origin. The case about to be described was typical.

Case No. 4. A man of 33 years of age was wounded in 1943 when he received superficial injuries in the right parietotemporal and occipital regions. Foreign bodies were removed shortly after wounding, and following the

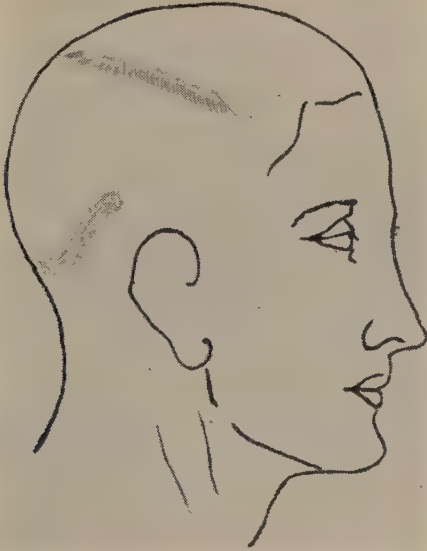


Fig. 3.

Sites of the granulomatous masses in Case 4.

excision and closure uninterrupted recovery permitted a return to his unit in the short period of three weeks. All went well until six to eight months before his coming under the observation of the author when headache and dizzy spells commenced. The headache consisted of a dull aching pain referred to the wound sites. No aggravating factors to the pain could be recognised. His dizzy spells referred to a sensation such as that induced by mounting ladders. For four months before appearing he had noticed swelling in the region of the scars.

On examination two linear masses were palpable, about 8-10 cm. in length, about two-and-a half centimetres across at their bases, and half that depth. Firm in consistency, immobile on the cranium, not unduly tender, their nature was uncertain. The blood W.R. was negative, and no body injury could be discerned on radiographic examination.

The man was anxious for removal of the swellings. Accordingly exploration was decided upon, but on making a minor incision a firm greyish mass was encountered, a mass of the consistency of unripe pear. A portion of tissue was excised for biopsy, then the incision closed. Since this appeared to be a granulomatous mass the effect of iodide by mouth was considered worthy of trial, the preparation chosen being Mercury and Arsenic Iodide (Donovan's Solution). Within one month the masses had disappeared.

The microscopic report stated "Section shows granulomatous nodules under the epithelium of the scalp. There are very numerous foreign body giant cells, some of which contain foreign bodies. The nodules are embedded in firm hyaline scar tissue. There are also striated muscle fibres included in the scar tissue".

Fortunately this is an uncommon experience. The reaction in this case demonstrates the irritating properties of the sulphonamide instilled into wounds as a precaution against sepsis. The rationale of the procedure is surely mistaken and this case reflects serious doubt on its use and efficacy. Throughout the war and since, the writer has never been convinced that any advantage could be gained by the introduction of sulphonamide powder into wounds. Certainly the incidence of infection has not been unfavourably influenced in consequence. Indeed, excision of devitalized tissue and proper debridement have met with desirable results.

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On Acoustic Neurinoma in Otological Diagnostics

By

STEEN JOHNSEN and HARALD K. KRISTENSEN

Acoustic neurinoma is a slow-growing tumor arising from the sheath of *Schwann* surrounding the 8th cranial nerve. Both acoustic and vestibular symptoms are dominating and early clinical features. Most patients with this affection therefore will seek otological treatment for their assumed ear lesion—even early in the course of the disease.

Fowler mentions as a well-known thing that these patients first consult the otologist and that the symptoms then do not differ very much from those of toxic acoustic neuritis or tubal catarrh. Consequently several patients with an acoustic tumor are submitted to some irrelevant treatment through a not inconsiderable length of time. Also *Cushing* has commented on the wanting knowledge of otologists concerning the classical symptoms of acoustic neurinoma, so that the patients often are given otological treatment for a long time in futile attempts to improve their hearing. As late as 1938 *Howie* stated that neurosurgeons still had this impression, and he emphasized that patients with intracranical tumors and with impairment of hearing as a predominant symptom get under neurosurgical treatment but too late.

Also in this country it appears as if such patients are not given operative treatment at the early stage of the lesion, as it is not the otological symptom, which at this juncture as a rule

has persisted for several years, that leads on to the correct diagnosis. This is not made until general symptoms of increased intracranial pressure or signs of functional impairment arise through the pressure exerted by the tumor on other cranial nerves in the vicinity. Here, too, it holds true that many patients for a considerable length of time have been treated symptomatically—for instance with repeated inflations, massage of the tympanic membrane, or with sedatives—under such diagnoses as: neurolabyrinthopathy, *Ménière's* disease, unclassified vertigo or tinnitus.

It is our impression that in some of the cases the correct diagnosis might have been made earlier with the results of the acoustic-vestibular examination as adjuvants if more attention had been paid to the possibility of acoustic neurinoma. We have therefore found it justified to make some remarks on the diagnosis of acoustic neurinoma in view of the acoustic and vestibular findings—on the basis of a case record material from the Neurosurgical Department comprising 81 patients with verified acoustic neurinoma.

MATERIAL¹

From 1934 to 1947 the diagnosis of acoustic neurinoma was made on 81 patients by operation, and verified by histological examination of the tumor. A majority of the patients were operated on in the period of 1937 to 1947. Acoustic neurinoma is not an altogether rare affection. According to *Cushing*, it makes 6 % of intracranial tumors, according to *Nylén* 10 %. Among the first 1,000 cases of intracranial tumors treated operatively in the Neurosurgical Department 7.2 % were acoustic neurinomas (*Busch*).

The sex distribution in this material was 58 women and 23

¹ To Dr. Jens Kragh, Chief Physician to the Dep. of Otology of the Military Hospital, we are greatly obliged for access to the hospital records in those cases in which the patients had been examined in this clinic.

men, which is in keeping with most previous reports, showing that the lesion is somewhat more frequent in women than in men.

The age distribution in our material was as follows:

10-19	20-29	30-39	40-49	50-59	60-69	70-79
3	4	20	20	24	10	0

The age given here was that of the patient on admission, not their age at the onset of the lesion. In this material, as will be noticed, no patient was 70 years or more. Presumably it is due to the circumstance that here we are dealing with a material of operable cases, and naturally this does not exclude that the lesion may be seen in patients over 70. Further, it will be noticed that more than two thirds of the patients were from 30 to 60 years old, with about the same number of cases in each of these three decades. Finally, it is seen that this affection is rare under the age of 30, and yet it occurs also in very young persons.

ANAMNESIS

The otological history of the patients includes unilateral hypacusia, which at the time of admission usually was described as complete deafness. In some cases the deafness had set in suddenly. In other cases it had been progressing gradually through several years without any remission. The history also included vestibular complaints which in several cases had been present as a constant uncharacteristic sensation of unsteadiness, as vertigo of a gyratory type or as wobbling on a ship's deck. These phenomena could be elicited by walking or rapid movements, but in some cases they had appeared as *ménieriform* attacks accompanied by a tendency to falling, without any known provoking cause. In some cases the vestibular symptoms were accompanied by nausea and vomiting.

A clinical picture consisting of one or more of the symptoms mentioned is in itself uncharacteristic and not particularly suggestive of an acoustic tumor. In order to get some impression

of which anamnestic symptoms might be of particular significance, we have looked into the frequency of each symptom in this material and also the time relation of these symptoms:

	Unilateral hypacusia	Tinnitus	Vestibular complaints
Percentage occurrence	89 %	41 %	89 %
Average duration	4½ years		1¾ years

Unilateral hypacusia is the most important complaint in the history of the patients because it is recorded in most of the present cases; it has been constant and of longer duration than the other complaints; besides, apparently it has been progressing rapidly to complete deafness. Whenever it has been noticed, it has been the initial symptom—except in three cases. Tinnitus is recorded only in half of the patients with impaired hearing. Hence, it is of lesser importance to the diagnosis, but in certain cases it makes the patient take notice of his impairment of hearing. Accordingly, tinnitus is often stated as arising simultaneously with the hypacusia, but also in several cases at a later juncture. In none of the present cases tinnitus was noticed prior to the impairment of hearing. The average duration of tinnitus is of no particular interest, as it was often found to be periodical, sometimes lasting only a few months in a case history of several years. Of the patients 10 % stated emphatically that they had never had tinnitus.

The vestibular complaints on an average appeared much later than the impairment of hearing, but on admission it was just as frequent as hypacusia. In most of the cases the impairment of hearing had been the only otological symptom through a number of years before the dizziness appeared (a difference of up to 10-15 years). In other cases the acoustic and vestibular symptoms commenced at nearly the same time. Finally, vestibular symptoms appeared initially in 3 cases. Half of the patients with vestibular complaints were troubled with nausea or vomiting, as a rule commencing simultaneously with the dizziness or later.

Thus in the history of the patients unilateral impairment of the hearing is an important complaint. It may be accompanied by tinnitus, but never preceded by it. After persisting for some years it becomes accompanied by vestibular symptoms, sometimes also nausea or vomiting. In some cases the affection commenced with simultaneous appearance of acoustic and vestibular symptoms. Only in exceptional cases do the vestibular symptoms appear initially.

On admission a good many of the patients complained of headache that had lasted for a couple of years and was localized to the brow or occipital region. A similar number of patients complained of dimness of vision or diplopia of only a few months' duration.

Cushing was the first to point out a certain regularity in the development of the disease. Corresponding to the origin of the tumor from the neurilemma of the 8th cranial nerve in the internal acoustic meatus or in the cerebellopontine angle, during its gradual growth the cochlear nerve is the first to be affected, later the vestibular nerve. On further expansive growth of the tumor, occipitofrontal headache appears, cerebellar incoordination and symptoms of functional impairment from the surrounding cranial nerves in a sequence determined by their relation to the 8th cranial nerve.

OBJECTIVE EXAMINATION

The present material does not allow of any particular working up of all the details of the acoustic function or the various aspects of the nystagmus, as the data recorded are stamped by the technique employed by the various examiners. In such a material the objective data can never be so systematic as in a clinical examination planned beforehand. Still, they may throw some light on certain main points of practical significance to the tumor diagnosis.

In most of the patients the acoustic function showed complete

deafness in one ear; this is evident from the schematic survey of the hearing given below, where abolished hearing means that the patient was unable to hear the speaking voice or shouting on masking of the other ear with Bárány's noise-maker:

Capacity of Hearing.

Abolished	< 2 m.	Whispering voice slightly lowered	Normal
58 = 72 %	19 = 23 %	2	2

Patients with abolished hearing of whispering and speaking voice were also unable to hear tuning forks or the monocord per air conduction or bone conduction. Weber lateralized to the normal side. Among the 19 patients with hearing of whispering voice within less than 2 m., 15 showed hearing of whispering voice within less than $1\frac{1}{2}$ m., and a good many of them showed hearing merely of speaking voice. They all showed signs of impairment of sound perception with lowering of the upper limit, shortened bone conduction, positive Rinne, and with Weber lateralization to the ear opposite to the tumor side; and besides, 10 patients showed a rise of the lower limit. The 2 patients with slight impairment of the hearing showed lowering of the upper limit. Furthermore, over one third of the patients showed slight perception deafness in the better hearing ear. In this connection it is to be mentioned that recently *Dix, Hallpike & Hood* have reported the observation that in some cases of acoustic neurinoma the perception deafness is not accompanied by the characteristic recruitment phenomenon.

VESTIBULAR FUNCTION

This heading covers examination for spontaneous, positional, and gaze nystagmus, and caloric irritability. All the patients were examined for caloric reaction and spontaneous nystagmus, some of them also for positional and gaze nystagmus.

Nylén has emphasized the value of examination for positional nystagmus, which in his own material was found in all the

patients but one. *Bruns* (1898) described a particular form of gaze nystagmus that may be seen in patients with acoustic neurinoma. It consists in coarse, slow, irregular movements towards the tumor side on gazing in the direction of the tumor side; fine, rapid, and regular movements away from the tumor side on gazing in the opposite direction.

We found spontaneous nystagmus in 40 patients (*i.e.*, 50 %). Of the remaining patients 17 showed postional nystagmus, and 15 gaze nystagmus. Thus nystagmus was found in altogether 72 out of 81 patients. The spontaneous nystagmus was most often horizontal-rotatory. The rapid phase of the nystagmus was preponderantly directed towards the tumor (35 of 40). In 5 cases this phase was directed contralaterally, and 5 patients showed vertical nystagmus.

The material does not allow of any detailed description of the postional nystagmus as to the direction of the movements elicited and the eliciting postures of the head. The gaze nystagmus was most often of the *Bruns* type.

The caloric irritability was examined either by injection of about 20 cc. water (26° C.) and following registration of the latent period before the commencement of the nystagmus; or by means of continuous flushing with water of 30° until the nystagmus appeared, and the latent period was recorded here, too. For practical reasons we have divided the results of this test into 3 groups: (1) abolished, (2) lowered, and (3) normal caloric reaction, with the following distribution of the findings:

Caloric Tests.

Reaction abolished	Lowered	Normal
62 = 75 %	6	13 = 16 %

Thus unilateral abolition of the caloric reaction was found in three fourths of the patients. It is obvious that such a specific symptom is of value to the diagnosis. But it must be kept in mind that lacking caloric reaction may be encountered also in other forms of tumors (meningioma, epidermoid, hemangioblasto-

ma) localized to the cerebellopontine angle, besides in cystic arachnoiditis in this region. Abolished caloric reaction is known also as a symptom in disseminated sclerosis, encephalitis and cerebrospinal syphilis. Finally, cases have been described of unilateral isolated loss of vestibular irritability from no demonstrable cause.

Even though unilateral loss of the vestibular function is the rule in acoustic neurinoma, the reaction is normal or only slightly impaired in some cases. Corresponding to the disturbances of the acoustic function on the side opposite the tumor, *Maybaum* states that it is possible with a special technique to find abnormal reactions in the vestibular function on the "normal" side. Diagnostically, however, these changes are of minor significance in comparison to abolition of the reaction on the affected side.

COMMENTS

The typical otological findings in acoustic neurinoma are complete unilateral deafness, total loss of vestibular functions on the same side, and nystagmus in one or more of the three forms mentioned, but all these symptoms need not be present at the same time. Neither normal caloric irritability (13 patients), absence of nystagmus (10 patients), nor normal hearing (2 patients) excludes this diagnosis. In one case even the acoustic and vestibular functions were normal. Between the cases with typical objective otological findings and the cases with normal function there are some cases with varying degrees of impairment of the vestibular and acoustic functions.

Now the question is whether the typical acoustic and vestibular changes are present at an early stage of the lesion when the patient seeks otological advice on account of impairment of hearing or tinnitus, so that an examination already at this juncture may arouse suspicion of acoustic neurinoma, calling for thorough neuro-ophthalmological examination.

Judging from the present material, these symptoms may be demonstrated even very early in the course of the lesion. Thus, in a few case records, it is stated that signs of abolished acoustic-vestibular functional capacity were found at an early juncture. Furthermore, on separation of patients without choked disk (patients at an earlier stage of the lesion than the remaining ones), the objective changes have been found percentally just as often in this group as in the total material.

This review of the present material has shown that in particular it is the abolished caloric reaction that arouses suspicion of the presence of an acoustic neurinoma.

In practice, however, it is impossible to perform a caloric test on all patients complaining of impairment of the hearing or tinnitus. But, when we meet with a patient between 30 and 60 years showing unilateral abolition of the hearing or pronounced unilateral perception deafness, he ought to be examined for spontaneous, positional, and gaze nystagmus, and if one of these forms of nystagmus is present, a caloric test should be performed.

If a patient complains of dizziness, and one of the three forms of nystagmus can be demonstrated, a caloric test is likewise indicated.

These examinations may be supplemented with examination for cerebellar ataxia (walking test and Romberg's test), corneal sensibility and facialis function—in particular as cerebellar ataxia and disturbance of the corneal sensibility are early symptoms, which in our material were found in respectively 63 % and 85 % of the cases. Impairment of the facialis function was found in 32 %.

In doubtful cases X-ray examination of the *pori acustici* may be of value. For this purpose, as stated by *Bager*, the *Towne* projection is particularly suitable, as—in contrast to the *Stenver* projection—it presents both *pori acustici* on the same film.

In conclusion it should be emphasized that the diagnosis cannot be made solely on the outcome of the otological examination. On the other hand, the otological examination is of great

importance to the diagnosis of this particular form of tumor, as even small deviations from the normal may indicate a more thorough neurosurgical and ophthalmological examination for further establishment of the nature of the affection.

SUMMARY

On the basis of a material comprising 81 acoustic tumors verified by operation and histological examination, the authors emphasize that most of these patients were first seen by otologists.

The acoustic and vestibular symptoms are recorded, and stress is laid upon the importance of the caloric test.

Finally, it is discussed when this test ought to be performed in order to refer any patients suspected of an acoustic tumor to additional roentgenological, ophthalmological and neurosurgical examination.

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Some Radiological and Neurosurgical Aspects of Tuberous Sclerosis

By

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The vast literature on tuberous sclerosis (t.s.) is in striking contrast to the rather rare occurrence of the condition. The reason for this discrepancy lies in the 'protean' character of this disease, which can affect different systems of the body and has thus attracted the attention of many workers in various special fields. Furthermore, the very nature of this condition has aroused many discussions, not only about its own pathological significance and classification, but also about the more general and still unsolved problem of origin and cause of tumour. To some, at least, t.s. has offered a proof that Kohnheim's famous theory was correct.

Historical reviews of the slowly growing knowledge of t.s. can be found in many publications (Globus 1932, Critchley and Earl 1932, Ferraro and Doolittle 1936, Ross and Dickerson 1943 and so on); there is, therefore, no need to do more than to consider this aspect of the subject very briefly.

As one would expect, the first reports were mainly based on necropsy material; psychiatrists and neurologists next studied the condition being mostly interested in t.s., while they in turn were followed by the skin specialists (Pringle) who were attracted by the adenoma sebaceum, which is so often present.

In 1908 Vogt described t.s. as "a form of idiocy", but a few years later (1914) Schuster pointed out the occurrence of 'Klinisch abortiver Fälle'—('formes frustes'), in which mental retardation and epileptic fits played but a minor rôle.

Very much later it was recognised that skin changes too can be lacking and that thus all main clinical features of t.s. may be absent in an undoubted case of the disease.

Incidentally, Schuster described at the same time the occurrence of intraventricular tumours in cases of t.s., but this was of academic interest only at a time when air-studies were yet unknown and surgical removal of such a tumour seemed hardly feasible. In the early twenties the ophthalmologist entered the field (van der Hoeve), followed by the general surgeon and urologist, who came to know that certain tumours of the kidneys can occur in t.s. and demand surgical intervention.

In 1924 a Swedish author, Marcus, was the first to describe X-ray changes in t.s. and his work in this field was elaborated by other Scandinavian writers. The neurosurgeon entered the arena rather late, not with much success, as will be seen, and though it is not likely that surgery will ever achieve very much more in these cases, none the less it might be worth while to consider those details, which could be useful to those who have to deal with these cases.

It may be advantageous to consider successively

- 1) cases showing the 'classical triad'.
- 2) 'formes frustes' and
- 3) cases with signs of increased intracranial pressure.

I.

The 'classical triad' of mental retardation, epileptic fits and adenoma sebaceum of the face, can hardly be mistaken.

If present, retinal phakomata, typical X-ray findings and proof of familial heredity will but confirm the diagnosis.

Three 'classical' cases were observed during the last few years by the present writer, and will be shortly described.

Case 1. Miss S. R. S., aged 22, was seen in 1944. She had seven brothers and sisters, all of whom were perfectly healthy. At the age of 2 weeks she had the first epileptic attack, which was followed by others at rather long intervals.

She did very badly at school and was later unable to learn any useful occupation.

At the age of 15 adenoma sebaceum developed in the face and was treated, with little success, by a dermatologist. On examination no neurological ab-

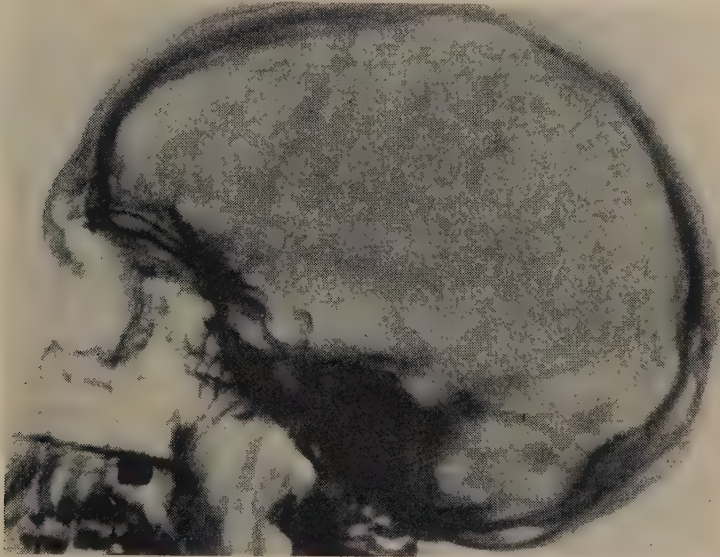


Fig. 1.

normalities were found except mental retardation; the fundi did not show retinal phakomata. X-ray examination showed some scattered small calcified spots, all situated on the left side, and also striking changes of the skull wall, which were considered by the radiologist, Dr. Gray, to be dense new bone formation of both tables with a narrow translucent zone between them, together with patchy sclerosis in the parietal bones (Fig. 1).

When this patient was re-examined, in 1949, no further signs could be found; the mental condition had remained unchanged, the epileptic attacks came on at a rate of 1-2 a week. X-rays of the skull were similar to those taken in 1944, hands, feet and lungs showed no radiological abnormalities.

Case 2. Mr. J. S., aged 22, was seen by Professor G. Jefferson and the present writer in 1944. He had two perfectly normal brothers and came from a healthy family. His mental retardation was the first abnormality observed by his parents, followed after a few years by the development of adenoma sebaceum faciei; later petit-mal attacks occurred, but major attacks with generalised convulsions

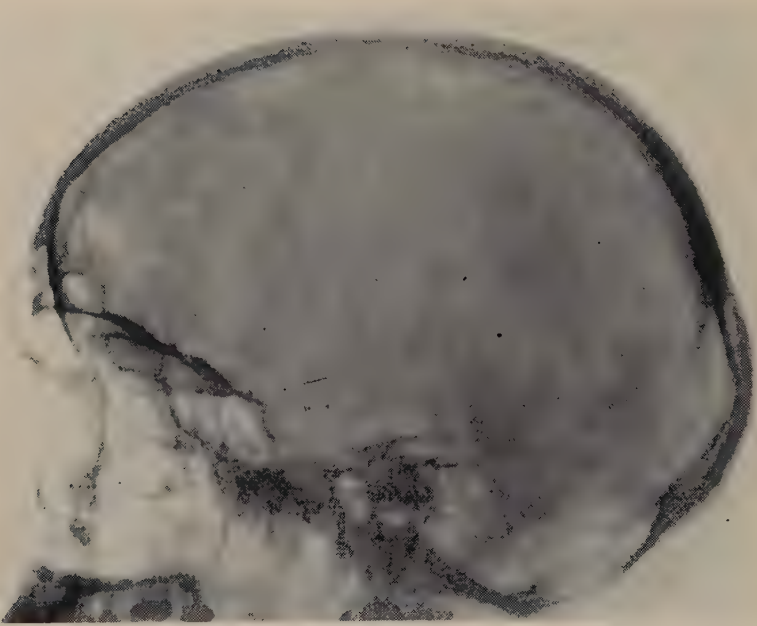


Fig. 2 A.

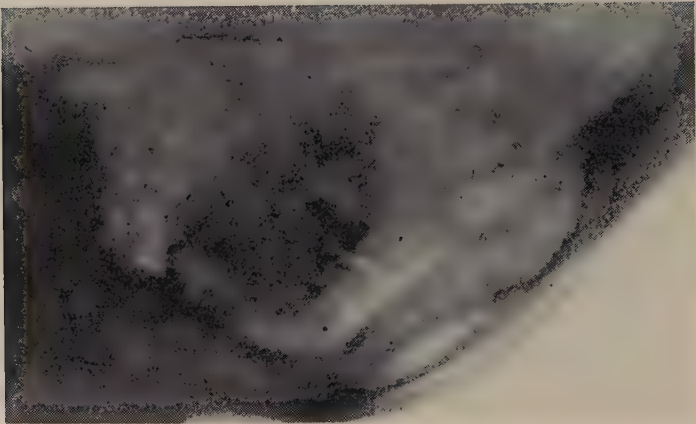


Fig. 2 B.

started at the age of 15, coming on once or twice a month from that time onwards.

He was a bad scholar and unable to do any useful work. Apart from his mental impairment no neurological abnormalities were found; no retinal phakoma was seen.

Electroencephalogram showed general dysrhythmia. X-ray examination revealed several small calcified spots, mainly in the parietal region, lying on both sides of the midline; in the cerebellar fossa a peculiar calcification with a ribbed pattern was observed, which seemed to lie on the surface of the cerebellum (Fig. 2 A and B).

This patient was seen again in 1949; he had been taking luminal regularly and had been free from epileptic attacks during the last four years. He had shown an interest and skill in piano playing and his parents hoped he might later on earn a living in this way. Neurological and radiological findings were essentially the same as in 1944.

Comment. It is, of course, well known that the cerebellum can also be affected in t.s., but this is not very common (Bielschowsky, Pollak, Liber and others). Cerebellar nodules can be calcified, but radiologically visible nodules are extremely rare as far as one can judge from the literature.

The X-ray changes in the cerebellar fossa of the patient just described, have apparently not been observed before.

Case 3. Mr. E. J., aged 30, was seen by Professor G. Jefferson and the writer in 1945. He had been mentally defective from birth and liable to get generalised epileptic attacks since early childhood; the frequency of these attacks had lately increased and he had become unmanageable.

Examination showed typical adenoma sebaceum of the face, which together with the typical history made the diagnosis of t.s., certain. No retinal abnormality was seen.

The parents of this patient were advised to send him to an institution for mental defective cases; this was done, but he died about a month after admission. Necropsy was not performed.

The clinical features of these three cases are quite typical and need no further discussion, but a few words about the radiological changes in t.s., may be added.

H. Marcus (1924) was the first to describe calcified areas of the size of a bean or pea, visible on the X-ray pictures of the skull of a patient suffering from t.s. Dalsgaard-Nielsen (1935) drew attention to the changes of the skull wall. Further contributions were added by Macdonald (1935), Gottlieb and Lavine (1935), Kveim (1937), Yakovlev and Corwin (1939), Heublin, Pendergrass and Widman (1940), Anderson (1942), Ross and Dickerson (1943)

and others. Dickerson (1945) proved by necropsy and histological studies, that the patchy zones of increased density in the skull wall were due to hyperostosis of the inner table and of the trabeculae of the diploic spaces; furthermore, the calvaria was diminished in thickness and the normal marrow replaced by fat, rendering the involved areas more translucent to light. Many, if not all, of these sclerosed 'islands' overlay tuberos nodules in the cerebral cortex. These zones of sclerosis were never seen in patients below the age of puberty, but of 17 patients at or after the age of puberty, 13 showed these changes. Hall (1940) suggested that the patchy zones of increased density of the calvaria were seen only in patients with evidence of neurofibromatosis as well as t.s.; this view, however, is not generally accepted.

In addition to these changes of the calvaria small intracerebral calcifications may be present. However, these small calcified spots which lie in the brain substance itself, invariably in the nodules, either attached to the ventricular walls or near the cortex, show no peculiar form, size or distribution; they are, therefore, not pathognomonic for t.s. unless they occur together with sclerosed patches of the skull wall. Ross and Dickerson (1943) found that 20 patients out of 25 showed radiologically many small discrete areas of calcification throughout the brain substance; in 2 patients such areas were seen in the cerebellum. Illing (1943) stated that only 7 of his 21 patients showed small calcifications, when examined radiologically.

Of the 6 patients in this series 5 were X-rayed and 4 of them showed either single or multiple small intracerebral calcifications (see Figs. 1, 2, A and B, and 4).

These calcified spots can be observed rather early in childhood; in one of Apley's cases they were found at the age of $5\frac{3}{4}$ years, but they had not been present when the child had been examined at the age of $3\frac{3}{4}$.

The question arises if the diagnosis of t.s. could be made by X-ray examination alone. If the changes of the skull wall de-

scribed above are present either alone or together with small scattered calcified spots, the diagnosis could be made with a great probability of being correct. The occurrence of multiple small calcifications, still less a single one, is not sufficiently characteristic for t.s. as similar abnormalities can be observed in other conditions too.

A solitary calcification, round shaped and of moderate size (as observed e.g. in case 5 of this paper, in case 1 of Puech) can be observed in many different conditions beside t.s. and does, therefore, not contribute to the diagnosis.

Multiple scattered calcified spots are also seen in other conditions, e.g. a case of multiple telangiectases of the brain, recorded by Michael and Levin showed such changes. Multiple meningiomata, if calcified, can give similar pictures; the case of Cohen, however, shows rather massive shadows produced by multiple intraventricular meningiomata and the same is true of some cases reported by Vestergaard from Dr. Busch's clinic, but if they had been X-rayed at an earlier stage these patients might have shown small calcified spots, indistinguishable from other lesions.

In contrast, the calcifications in Sturge-Weber's disease are absolutely characteristic; symmetrical calcifications usually limited to the basal ganglia can occur in many conditions (Eaton, Camp and Love), but are different from those observed in t.s.

Calcified subdural haematoma can form punctate deposits, which, however, are adjacent to the inner table of the skull (Dyke and co-workers). Tuberculomata produce as a rule rather massive shadows; haemangioma calcificans, an epileptogenic lesion, recently described by Penfield and Ward (1948), can produce more than one calcification (case 3), but curiously enough, in all cases one temporal lobe only was affected.

Finally in cysticercosis and toxoplasmosis small scattered intracranial calcifications can be observed. Cysticercosis has become rather rare now (Lysholm, Brailsford, Dyke and co-workers, and others), though not in Latin-America (nor in some

Asiatic countries. In this country Dixon and Hargreaves (1944) examined and followed up no less than 284 cases of cysticercosis, nearly all of them soldiers (except 2 female patients), who had served abroad, most of them in India.

Of these 284 cases 212 showed radiological changes, mostly calcified cysts in the muscles; 32 showed evidence of calcified cysts in the brain, but only 2 of these had no calcified cysts in the muscles.

Dixon and Hargreaves point out that these changes if studied with a magnifying glass, show often a dense calcification in the scolex surrounded by a calcified cyst wall. Thus, careful study of the type of calcification would help to diagnose cysticercosis in the unlikely event of the absence of concomitant muscular calcifications.

Toxoplasmosis almost invariably produces calcifications, usually 2 mm in diameter, which are exceptionally restricted to one side (Dyke and co-workers, 1942).

It is, however, a very rare disease in human beings and no more than 50 cases were on record in 1948 (Binkhorst). On the other hand it is not without interest that Lichstein and Solis described as 'familial tuberous sclerosis without adenoma sebaceum', what Merritt and Aring, and Koch suggested was toxoplasmosis. Some features of toxoplasmosis in those patients, who survive the acute phase, like generalized epileptic fits or petit-mal seizures, retardation of speech development and mental deficiency (Wolf, Cowen and Paige, 1942) occur also in t.s., but perhaps the most essential clinical difference is that on examination of the fundus chorioretinitis was observed in all but 2 cases on record (Binkhorst), whereas in t.s., if retinal changes are present, phakomata occur.

Again, the rarity of toxoplasmosis must be underlined. In this country the first case was described a short while ago (December 1948) by Jacoby and Sagorin. And though more cases were reported in the Scandinavian countries, at the present time toxoplasmosis is a very interesting, but extremely remote diagnostic

possibility, in patients with mental deficiency, brain calcifications and epileptic attacks.

Finally, air-studies can reveal the presence of intraventricular tumour nodules and thus make possible a correct diagnosis in cases with incomplete symptomatology. Ross and Dickerson observed such small tumours on encephalograms in 35 % of their 25 cases. Similar observations were reported by Drake (1934), Berkwitz and Rigler (1934), Kveim (1937), De Jong (1936), Ruggeri (1939), Heublein, Pendergrass and Widman (1940), Anderson (1942), Radovici and Schwartz (1948). Illing's investigations (1943) are particularly valuable as his 21 cases were later on verified by necropsy; in 11 cases definite intraventricular tumour nodules were observed radiologically, in 5 further cases the pictures showed probable nodules. It must be added that in some cases hydrocephalic enlargement of the ventricles only was observed. Ventriculographic findings in cases of t.s. with increased intracranial tension will be discussed later.

II.

In patients who show but an incomplete syndrome of t.s. diagnosis may be difficult or even impossible; this is especially true of infants and children, who have not yet developed the typical skin-changes (Illing, Globus and Selinsky, 1935). As to 'formes frustes' in t.s., Critchley and Earl have mentioned the following possibilities:

- 1) Adenoma sebaceum alone.
- 2) Adenoma sebaceum with epileptic fits but no mental changes.
- 3) Adenoma sebaceum with cerebral tumour.
- 4) Visceral tumours alone (including retinal tumours).

Globus, Strauss and Selinsky (1932) described a number of cases showing no clinical signs of t.s. at all, but suffering from fits or cerebral tumour; t.s. was only confirmed by necropsy. Further cases of this kind will be mentioned later.

Stewart (1935) reported a case of a married woman, aged 21, of normal intelligence without adenoma sebaceum, who died

in her first epileptic attack, post mortem examination showing cerebral changes typical of t.s.

Van der Hoeve discovered a retinal phakoma in an otherwise apparently normal patient, whose 5 brothers and sisters suffered from advanced t.s.

F. B. Walsh (1947) observed a senior university student, mentally alert, who never had an epileptic attack, but showed adenoma sebaceum and typical changes of the fundi.

In such cases X-ray examination may be helpful.

The occurrence of mixed formes of the different 'neuro-cutaneous syndromes' can only be mentioned.

III.

It has been known for many years that patients suffering from t.s. can develop signs of increased intracranial pressure, which are almost invariably due to a tumour, nearly always situated in the ventricles. In some cases the tumour signs can obscure the clinical signs of t.s. to such an extent, that the correct diagnosis is not established.

In 'abortive' forms the anatomical alterations in the brain may be so meagre, that they escape attention at the post mortem examination unless very carefully sought for (Globus 1932).

The overwhelming majority of tumours in t.s., which are on record, were intraventricular ones, situated in the strio-thalamic region, near the sulcus terminalis, in intimate relationship to one or both foramina of Monro, blocking more or less completely one or both of them and thus producing hydrocephalus; nearly invariably the 3rd ventricle is also invaded by the tumour, often being completely obliterated in its anterior part.

A good example was made available to the writer by the courtesy of Dr. G. Stewart Smith (late of Manchester). The specimen (Fig. 3), the brain of a 23 year old patient suffering from epiloia, shows a cherry-sized tumour in the left anterior horn, originating from the strio-thalamic region and the lower part of the septum lucidum, which is displaced to the other side;

this tumour, lying just laterally and in front of the foramen of Monro, had caused a partial block and produced a moderate, asymmetrical hydrocephalus. A smaller tumour is present on the right side, but slightly further away from the foramen inter-ventriculare.

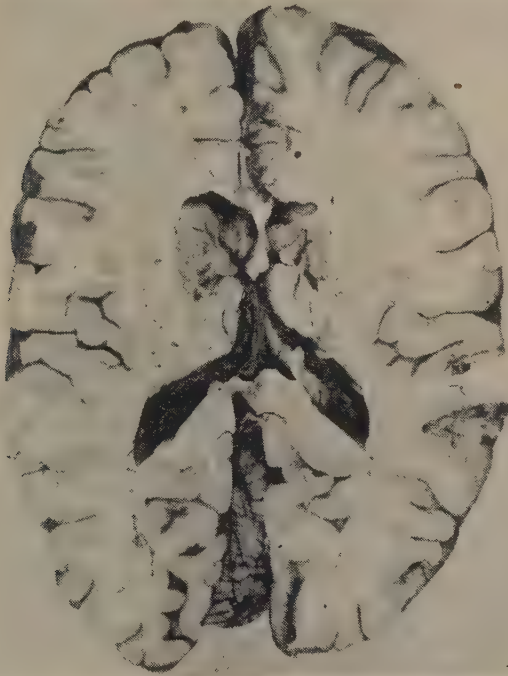


Fig. 3.

TUMOUR CASES OF THIS SERIES

Three further cases of tumour in cases of t.s. are at the present writer's disposal, 2 of them verified, the third, unfortunately, unverified.

Case 4 was observed in this department and previously described by Twining (1939) and by Jefferson and Jackson (1939), which makes it unnecessary to repeat the whole story here. The patient, a girl aged 7, with no trace of abnormal cutaneous markings on the face or body, was mentally backward and had been suffering from unilateral fits since the age of 4 months. On admission, signs of increased intracranial tension, retinal phakoma on one side, and hemi-

paresis were present. X-rays showed a small rather dense calcification of the size of a pea, 5 cm. above the sella, well to the left of the midline. Ventriculography failed to show the 3rd ventricle but revealed asymmetrical hydrocephalus and a tumour shadow obstructing the left foramen of Monro, apparently arising from the floor of the left lateral ventricle (Twining). Operation was not performed and the child died 8 days after ventriculography. The lesion in the 3rd ventricle was described by Dr. Greenfield as 'embryonal tumour', the intraventricular extensions were considered as non-neoplastic. The brain showed in addition changes typical for t.s. (Several illustrations concerning this case are contained in the papers mentioned above).

Comment. The difficulties of arriving at the correct clinical diagnosis in this case are obvious; however, more is known about lesions of this kind at the present time, and a tumour in such a situation, in a young mental defective and epileptic patient, would probably make one think of t.s.

The diagnostic difficulties are, of course, still greater, if a patient shows signs of a cerebral tumour only, as the following example shows.

Case 5. This case was observed and X-rayed by Dr. A. Bannwarth, to whom the writer is greatly indebted for his permission to mention the history here. The patient, aged 44, had never been seriously ill prior to admission to hospital owing to signs of increased intracranial tension. Examination revealed bilateral papilloedema, but no localising signs. No skin changes were present, the patient's intellectual level was normal and he had never had an epileptic attack.

X-ray examination showed a few calcified spots in the parietal area; ventriculography showed asymmetrical hydrocephalus, the right ventricle being larger than the left, the septum lucidum being displaced towards the left side. A tumour shadow was visible, occupying the right wall of the 3rd ventricle partially blocking the right foramen of Monro and projecting into the right lateral ventricle (Figs. 4 and 5).

The site of this tumour and the scattered calcified spots, both considered as typical for t.s., led to the correct clinical diagnosis. Operation was not advised. The patient died some time later; examination of the brain (Prof. W. Scholz) confirmed the diagnosis of t.s.

Case 6. M. B., a girl aged 9, was seen by the present writer at the Booth Hall Children's Hospital, Manchester, in 1945, at the request of Dr. W. H. Patterson, who had already made the diagnosis of cerebral tumour. The child was, therefore, transferred to the Neurosurgical Department of the Manchester

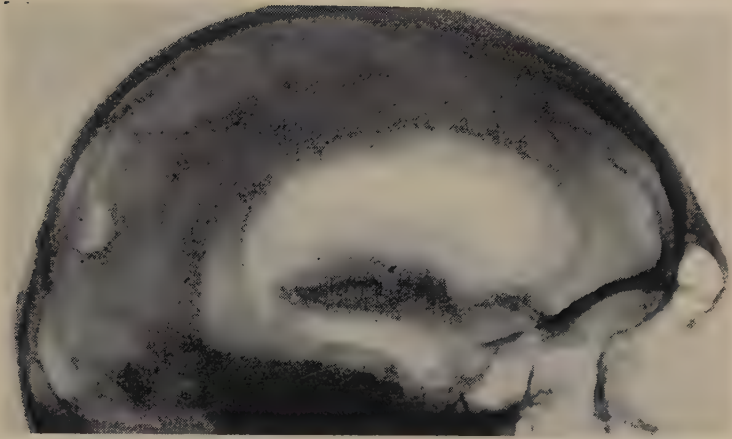


Fig. 4.

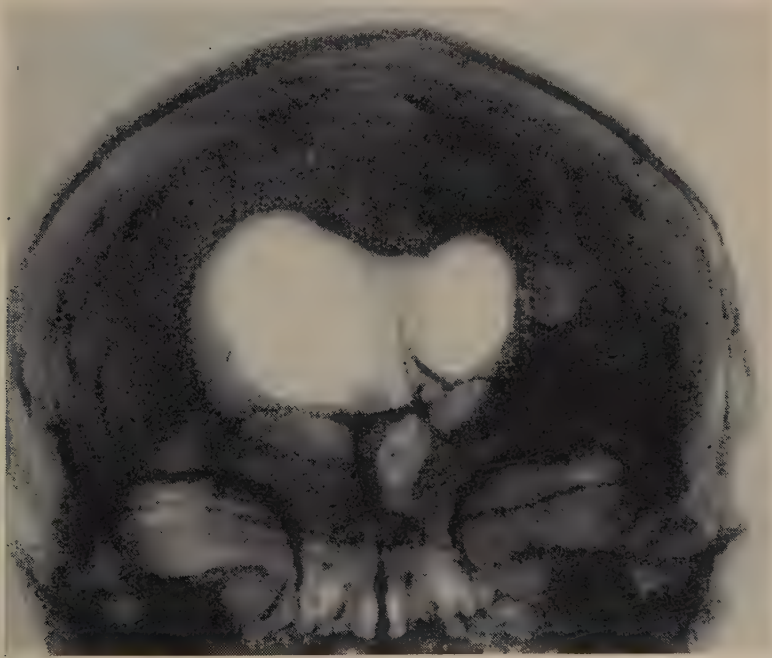


Fig. 5.

Royal Infirmary. The child had previously been perfectly healthy. On examination, bilateral papilloedema, Macewen's sign, left-sided hemiparesis and definite hyperpathy on this side were found.

X-rays of the skull showed wide separation of the coronal suture. Ventriculography was carried out on the left side first and showed the left and part

of the 3rd ventricle only; when the right ventricle was punctured, yellow c.s.f. escaped (containing 450 mgm⁰% protein, against 20 mgm⁰% on the left side). Ventriculograms showed a filling defect in the upper anterior part of the third ventricle and a nodular tumour shadow obstructing the right foramen of Monro and protruding into the right anterior horn (Fig. 6).

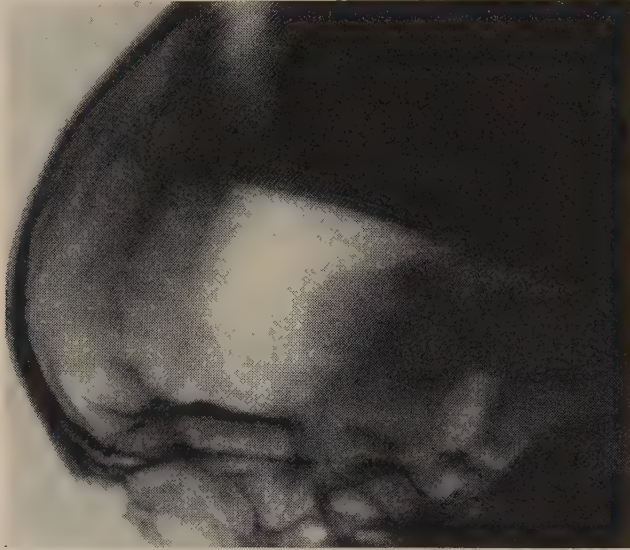


Fig. 6.

The tumour was considered inoperable, as it was assumed that the thalamus and internal capsule were infiltrated; therefore, right subtemporal decompression was carried out, followed by X-ray treatment.

Three months later the girl was seen again, she was feeling quite well, the subtemporal decompression was not tense, the hemiparesis had somewhat improved. A few weeks later the girl started to have epileptic fits; in May 1946 she became suddenly comatous after such a fit, was sent to a hospital, but died shortly afterwards, nearly 9 months after operation. Autopsy was refused.

Comment. In retrospect it seems that the Torkildsen procedure would have been more suitable and might have given the patient a better chance. Unfortunately, the final diagnosis must remain uncertain in this case, but the 'typical' site and also the shape of the intraventricular tumour is certainly very suggestive of t.s.

REVIEW OF LITERATURE

A review of the relevant literature (which for several reasons is not complete) reveals a rather big number of cases of t.s. with intraventricular tumour, situated in the region of the foramen of Monro, and producing increased pressure. Even more interesting is the fact that quite a few of these cases had no clinical signs of t.s.

The 'typical' tumour localisation was observed in the cases of: Kaufmann-Fischer (1911), Schuster (1941, case 1), Berliner (1921), Bielschowsky (1924), Meduna (1930), Creutzfeld (1932, 2 cases), McConell (published by Critchley and Earl, 1932), Dandy (1932, case 6, group II). The case of Cook and Meyer (1934/35) had a very large tumour 'in the centre of the brain', with a pedicle in the strio-thalamic region, which means, of course, that this was the point of origin.

The patient became suddenly comatous and died 4 hours later, the cause of death being haemorrhage into the tumour.

Further cases were published by Ferraro and Doolittle (1936, cases 16 and 17), Liber (1938), Koch and Walsh (1939, most probably 'typical' site), Stender and Zülch (1943, 8 cases), Krug and Echlin (1944).

Globus has made quite a number of valuable contributions to the subject under discussion (Globus 1932, Globus, Strauss and Selinsky 1932, Globus 1938, Globus 1941, Globus and Kuhlenbeck 1942). In the publication with Strauss and Selinsky (1932) Globus quoted 11 cases; not all of these patients suffered from increased intracranial pressure caused by the tumour, but apparently 5 only (cases 1, 3, 5, 7, 9); of these 5 patients 3 showed intraventricular tumours at the 'typical' site.

The patient, recorded by Lhermitte, Heuyer and Vogt (1935) harboured a glioma of the size of a cherry near one foramen of Monro, but suffered also from tuberculous meningitis the latter probably being the cause of death. To this list the 3 verified cases of this series should be added.

A more thorough search of the literature would yield a few more cases.

A small but most important group consists of cases of t.s. with pressure signs, caused by tumours not situated in the neighbourhood of the foramen of Monro, e.g. cases of Globus and co-workers (1932; 2 cases, tumour of the frontal and occipital lobe respectively); Stevenson and McGowan (1937; with chiefly cerebellar involvement, producing stricture of the iter and simulating a lesion of the quadrigeminal plate); Puech (1945, case 2, frontal tumour, not invading the ventricle, combined with serous meningitis).

A few cases of t.s. with signs of increased intracranial pressure have been recorded, in which the site of the lesion is not stated (Bychowski (1931), Hall (1940), Moolten (1942)).

There are on record, too, quite a few tumours of the strio-thalamic region in cases of t.s. reaching some size, but not producing increased tension, e.g. the most interesting case of Anderson (1942), and cases of Brushfield and Wyatt (1926), De Jong (1936) and others. These cases offer quite different clinical pictures and problems, and cannot be considered here any further.

This short review reveals quite clearly the great preponderance of tumours in the strio-thalamic region over those situated in other regions (30-odd cases against 4). It becomes also apparent, that amongst intraventricular tumours of all sorts the group made up of lesions in t.s. cases, occupies quite an important place.

More than a quarter of the cases mentioned above showed clinically no signs of t.s. at all (e.g. 4 cases of Globus, Strauss and Selinsky, 3 cases of Stender and Zülch, cases 5 and 6 of this series); others showed mild or incomplete forms of this disease only (e.g. case 5 of Stender and Zülch, case of Stenvenson and McGowan).

Some of the cases listed above, need further comment, above all the case of W. E. Dandy, recorded in his most remarkable

monograph on benign tumours in the third ventricle of the brain (1933, p. 64).

The story of this patient has been more fully reported and carried further by F. R. Ford (1946, p. 866) and by F. B. Walsh (1947, p. 1086). At the age of 3 this girl developed skin changes of the face, which, some years later, were diagnosed as adenoma sebaceum; she did poorly at school. At the age of 15 she developed signs of increased intracranial pressure and was subsequently operated upon by Dandy, who diagnosed clinically a third ventricle tumour, as X-rays had shown calcification in this region. At operation the right ventricle was entered and a tumour removed, which projected from the 3rd ventricle into the foramen of Monro. The tumour was thought to be of embryonal origin.

Four years after operation the patient was examined by F. B. Walsh. The skin lesion had been extensively treated and was no longer characteristic. The right fundus showed retinal phakomata typical of t.s. Mentally the patient was definitely subnormal, but she had no complaints and had had no fits.—It would appear, that Walsh saw this patient again at the age of 21, i.e. 6 years after operation, and that she was quite well then. This is a most excellent result, the best achieved so far in a t.s. case with intraventricular tumour.

Ford mentions also that Dandy removed tumours in the ventricles in *several* cases of t.s. with success, but gives no further details. However, Dandy's case 7 (1933, p. 71) shows exactly the same histological picture of a tumour considered to be of embryonal derivation; this lesion was found in a girl aged 12, and was situated mainly in the left anterior horn, attached to the corresponding foramen of Monro. This patient died some three weeks after removal of the growth.

In Dandy's book on tumours in the lateral ventricles (1934), case 9 (p. 95) concerns a girl, aged 9, with a similar lesion.

The tumour was attached to the medial wall of the left ventricle, just anterior to the foramen of Monro, and had produced

unilateral hydrocephalus. Removal of the lesion was followed by post-operative haemorrhage and death.

Dandy himself draws the reader's attention to the close histological resemblance of the tumours found in the 3 cases just mentioned.

The histories of these 3 patients (all of them children, harbouring tumours of practically identical localisation and structure) and the fact, that one of them was a classical case of t.s., force one nearly inevitably to the conclusion, that the other 2 patients were also cases of t.s.

Finally, cases 5 and 6 in Dandy's monograph (1934) show ventriculograms, highly suggestive of tumours found in t.s. as are some details of the histories. In one case, however, the specimen was lost, and in the other a different histological picture was found. Therefore, the question cannot be decided, whether nor not one or both cases belong to the group under discussion.

Stender and Zülch (1943) brought together a collection of 8 cases, examined and treated respectively by several neuropathologists, neurologists and neurosurgeons. They drew, once again, attention to the fact that one or even all so-called classical signs of t.s. can be absent; 4 of their cases showed the clinical features of the classical triad, 1 showed mental impairment, suffered from fits, but had no skin changes. Three patients showed tumour signs only and had been perfectly healthy prior to admission into hospital; these 3 patients were operated upon and all of them died.

Necropsy showed in 2 cases changes of the brain typical for t.s., the third case was considered to belong to this group, as the tumour showed the same histology as the others.

The main conclusions of Stender and Zülch are 1) that these tumours produce typical ventriculograms, and 2) that they show a peculiar and for t.s. tumours typical histological picture. As to the first conclusion, the authors themselves suggest—quite rightly—that ependymomata of the strio-thalamic region could probably

produce similar ventriculographic changes, though the occurrence of such a lesion is considered to be extremely rare.

It is true that such cases are not very common, but they do occur and some of them are on record; the verified ependymoma recorded by Ostertag (1936, p. 55 and 56) would have given a similar ventriculographic picture. Other gliomata too can produce similar ventriculographic pictures, like the astrocytomata described by Jefferson and Jackson (1939, case 12), Kessel and Olivecrona (1936, case 6) and others.

The gangliocytoma described by Kernohan, Learmonth and Doyle (1932, case 5) of a patient who died after ventriculography must have given the same picture, as far as one can conclude from the description of the brain at the necropsy. The second conclusion of Stender and Zülch will be discussed presently.

Last, but not least, Globus' contributions to the subject under discussion must be mentioned. Globus stressed again and again, that t.s. without the classical signs can occur and that in such cases, if they show signs of brain tumour, the correct diagnosis may be missed. Some of the cases of his extensive paper on these tumours (Globus, Strauss and Selinsky, 1932) were afterwards no longer considered to be t.s., others were later diagnosed differently, but this cannot detract anything from this author's merits.

Modifying Bielschowski's terminology, Globus considers t.s. as 'neurospongioblastosis disseminata' and finds that all active tumours in these cases are 'neurospongioblastomata'.

HISTOLOGY

The tumours under discussion have been differently diagnosed histologically and, reviewing some of the cases recorded, one finds the following designations: astrocytoma (McConnell's case, quoted by Critchley and Earl; Roussy and Oberling; Meduna, Liber); embryonal glioma (Dandy; Jefferson and Jackson); spongioblastoma (Cook and Meyer; Lhermitte and co-workers; Oster-

tag 1941, p. 408); angioglioma (Bergstrand); neurinoma (Puech and co-workers); 'mixed structure' (Ferraro and Doolittle, cases 16 and 17). Globus, however, finds that these lesions are invariably neurospongioblastomata, originating from the subependymal cell plate. Stender and Zülch assume that the histological picture of the intraventricular tumours is uniform, characteristic of and peculiar to t.s., so much so, that the microscopical findings suffice to diagnose t.s. Obviously, further observations are necessary before this view can be accepted.

SURGICAL CONSIDERATIONS

It goes without saying, that radical removal of gliomata arising from the strio-thalamic region involves great risks and will inevitably carry a high mortality rate.

The approach to the 3rd ventricle recommended by Busch (1944), would be helpful, if the main mass of the lesion is situated in the 3rd ventricle. But the danger of damaging the hypothalamus remains, and other surgeons like Torkildsen (1948), and Ward and Spurling (1948) pleaded for a more conservative attitude in cases of neoplasm in or near the third ventricle.

If the main mass of the growth is situated in the lateral ventricle extending only very little into the 3rd ventricle, the risk apparently is not much smaller. This is certainly true of the neoplasms in t.s. cases on record, as shown by the following review.

The patient, recorded by Kaufmann and Fischer, died from meningitis after operation had been attempted, some 40 years ago, when no means of exact localisation existed and neurosurgery was in its infancy.

Of the 5 cases of Globus and his co-workers showing pressure signs, 1 died after ventriculography, 3 were operated upon and died shortly afterwards.

Creutzfeldt's case 1 underwent puncture of the corpus callosum, with some relief, developed kidney troubles 4 years later, necessitating nephrectomy.

Dandy's case, quoted above at length, was successfully operated upon and alive 6 years later, though developing further signs of t.s.

Moolten's patient underwent nephrectomy at the age of 15 (for 'hamartomata'), developed signs of cerebral neoplasm at the age of 20 and died after decompression. Stevenson and McGowan's patient underwent 3rd ventriculostomy for obstructive hydrocephalus, but died 1 month later.

Of Stender and Zülch's series 5 patients were operated upon with 4 post-operative fatalities; the only survivor was handicapped by mental retardation and epileptic fits.

Echlin removed successfully a lesion of the strio-thalamic region, but the result of the operation was spoilt by a post-operative sinusthrombosis, which left the patient paraplegic and confined to a wheel-chair 26 months after surgical intervention.

Puech achieved successful removal of a true frontal tumour accompanied by localized serous meningitis in a typical case of t.s.

Luque and Pucheta recorded a case of t.s. showing intracranial hypertension, improved by surgical therapy¹.

In some cases removal of the neoplasm was considered inadvisable and palliative treatment carried out. Thus, in the case of Koch and Walsh, the neurosurgeon, A. W. Adson, advised against operation in view of the signs of t.s. present, and recommended X-ray treatment; the patient was still alive 9 months later.

The unverified case 6 of this series underwent subtemporal decompression followed by X-ray treatment and died 9 months after operation.

As one would expect, the results of radical removal of intraventricular gliomata are not encouraging. In view of a mortality rate of 80 % in their series of 5 cases, Stender and Zülch plead for a more conservative attitude.

¹ This publication (*Arch. neurocirc.*, Buenos Aires, 1, 83 (1944) is not available in this country; for this reason further details cannot be given.

As stated above, Torkildsen's ventriculocisternostomy is probably the most useful procedure in these cases, carried out on both sides, if necessary, and followed by X-ray treatment. It is self-evident that signs of t.s., if present, must influence the indication for operation.

CONCLUSIONS

Review of the literature and experience with the cases of this series justify the following conclusions: Gliomata in cases of t.s., nearly invariably situated in the strio-thalamic region, are by no means rare. If a patient suffering from t.s. develops signs of intracranial hypertension, he will much more probably harbour a neoplasm blocking one or both foramina of Monro than have a tumour elsewhere. If, on the other hand, air-studies reveal a lesion of the strio-thalamic region in a patient otherwise apparently quite healthy, t.s. should be suspected.

Radical operation has not been very successful and palliative treatment like Torkildsen's procedure followed by X-ray treatment promises better results.

The author's sincere thanks are due to Professor G. Jefferson, Dr. E. D. Gray, Dr. A. Bannwarth and Dr. G. Stewart Smith.

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On Exophthalmometry

*The result of 724 measurements with Hertel's exophthalmometer
on normal adult individuals.*

By

KARSTEN KNUDTZON¹

The exact measurement of the degree of protrusion of the eyes in various diseases first attracted attention in 1865, when the first exophthalmometer was constructed by *Cohn*; he measured the position of the vertex of the cornea in relation to the external margin of the orbit. It was not long before he abandoned this principle, however, and instead determined the distance between a frontal plane through the centre of the superior margin of the orbit and another through the vertex of the cornea and employed the terms positive and negative protrusion, according to whether the former frontal plane lay rearmost or foremost. He considered that the superior orbital margin was subject to fewer anatomical variations than the external orbital margin.

Quite a number of exophthalmometers have been devised since then. In most of them the external orbital margin is preferred as the fixed point (*Ambialet*, *F. V. Birch-Hirschfeld*, *Emmert*, *Gormaz*, *Hertel*, *Keyser*, *Lohmann*, *Luedde*, *Murphy*, *Snel-*

¹ Paper read before the Ophthalmological Society, Copenhagen, February 12th, 1949.

len, Trendelenburg, Weiss, Zehender), despite the fact that cranial asymmetry is not unusual in this region. The advantage of using it is that it is easy to localize, the skin covering being thin regardless of variations in the fatty layer of the body. A few authors measure exophthalmus in relation to a point on the bridge of the nose (*Arnold*), and others again employ a plane through the orbital adit (*Kestenbaum*). The use of stereomicro-meter measurements on stereoscopic photographs has begun in recent years (*Lobeck*), though this method is only of scientific interest and will not be practical for ordinary clinical purposes.

Otherwise, the various methods of measuring do not vary much in principle. Some work with a pointer system on a millimetre scale (*Emmert, Hasner, Keyser, Sattler-Hering, Volkmann, Zehender*); others have a spectacle frame with a millimetre scale on the arm (*Knapp, Trendelenburg*); a few use a cup on closed eyelids (*Coccius, Snellen*) or on the anaesthetized cornea (*Gormaz, Weiss*). With *Hertel's* apparatus both the scale and the profile picture of the cornea are seen in mirrors; in *Rollet & Durand's* modification of this apparatus the mirror is used for the cornea only.

With most exophthalmometers separate adjustments are necessary for each eye; with *Hertel's* (and *Rollet & Durand's*) the degree of protrusion of both eyes can be read directly after a single adjustment. All in all, this apparatus has so many advantages that it has become the most widely used exophthalmometer everywhere in the world. It is easy to handle, measurements take only a very short time (< 1 minute), and when correctly used its accuracy is adequate for clinical use.

Exophthalmometry in the clinic is of most importance in determining the relative measurements: the difference between the protrusion of the eyes of the same individual, and the variations of either eye in the course of a disease. Naturally, the absolute values are also of a certain interest, but in normal individuals they vary so greatly from one to another that very wide limits must be allowed for what may be called normal.

A few authors have tried to fix the boundaries of normal exophthalmometer measures. Their results were based upon a small number of measurements and varied considerably; see Fig. 1. (*Cohn's* measurements in 1867 with his own apparatus on 427 persons—healthy and ailing—are not included, because his values are shown in relation to a frontal plane through the superior orbital margin and therefore are not comparable with the results of other authors, who give the distance between a frontal plane through the external orbital margin and one through the vertex of the cornea).

There is also a good deal of variation in the records of the relative measures of the eyes of the same individual; most authors agree that normal people often have unequal measures for the two eyes, but the degree and the frequency differ considerably in the various reports (Fig. 1).

I have set myself the task of contributing towards a clarification of the question of the size-ratio of the absolute measures, their distribution and limitation, and that of the relative measures for the two eyes, the background being a large number of measurements taken with Hertel's exophthalmometer on normal adult individuals. These measurements were taken in the first half of 1948 in the outdoor ophthalmological clinics of the Copenhagen Military Hospital and the Rigshospital.

In the selection of subjects I attached importance to healthy, adult, not too old people. The great majority were men on military service; there were also a number of female nurses, as well as outdoor patients between 15 and 65 years. Persons with affections likely to cause changes in the position of the eyes, and those with refraction anomalies which merely in one eye exceeded 2.5 dioptries, are not included in the material. This being so, the material is not representative of a cross-section of the population, but a group of healthy adults, chiefly young individuals.

My measurements were taken from 362 individuals, whose age and sex distribution appears from Fig. 2. In the process I

Author	Year of publication	Exophthalmometer employed	Number of examined persons	Nature of individuals
Emmert	1870	The author's	200	All sorts except patients with Grave's disease of tumours in eye or orbit
Keyser	1870	"	—	Normal
Birch-Hirschfeld	1900	Sattler-Hering's	24	Normal, 9–72 years (in 9 ametropia –20 to +3)
Geraud	1912	Rollet-Durand's	41	24 normal, > 14 years 5 children 10–13 years 12 old persons 52–76 yrs.
Birnbaum	1915	Hertel's	120 males 30 females	Normal
Schlabs	1915	"	50	Normal
Woods	1915	"	200	Normal
Helmbold	1916	"	300 males 225 females	Normal
Lee	1930	"	324 males 76 females	6–53 years } 5–60 " } normal
Wagener	1934	"	200	Normal
Galli-Mainini	1942	Modified Luedde's	50	Normal
Soley	1942	Hertel's	23 males 42 females	Normal 19–51 years (average 32 years)
Gormaz	1946	The author's	—	—
Knudtzon	1949	Hertel's	263 males 99 females	Normal

Fig. 1.

Absolute values		Relative values		
Outer limits	Average values	Proportion with unequal values	Difference between eye measures	More protuding eye
9-20 mm	12-14 mm	93.5 %	up to 3 mm	—
9-18 "	At puberty 14 mm	rare	up to 2 mm	—
11.5-18 "	14 mm (in the 15 em- metrope persons: 12.7 mm)	10	0.5 mm in 5 1.0 mm in 5	right eye in 4 left eye in 6
11-16 "	13 mm	—	—	—
10-13.5 "	11.7 "	—	—	—
11-15.5 "	13.6 "	—	—	—
11-19 "	15 "	—	—	—
11-18 "	14.5 "	—	—	—
10.1-21 "	—	45	0.2-1.5 mm	right eye
—	12-14 mm	—	—	—
9.5-24.5 "	16.67 mm	—	—	—
9.5-22.5 "	15.68 "	—	—	—
8-21 "	14.4 "	—	—	—
	14.8 "	—	—	—
11-24 "	17.9 "	150	0.5-2.0	right eye in 139 left eye in 11
n 80% 15-20 mm)				
14-17.5 "	—	—	—	—
11.5-20 "	15.9 "	—	—	—
> 12 "	14-16 mm	—	—	—
11-24 "	17.1 mm	203	0.5-1.0 mm in	right eye in 130
12-22 "	16.8 "	(56 %)	191, > 1 mm in 12	left eye in 73

A horizontal line in a column indicates incomplete information.

aimed at pressing the supports of the Hertel apparatus as firmly as possible against the external orbital margins without causing the subject too much discomfort. When making the reading I requested the subject to fix my eye which was kept in the same sagittal plane and horizontal plane as the middle of the mirrors watched. In most cases I have also noted the measures shown on the apparatus for the distance between the external orbital margins.

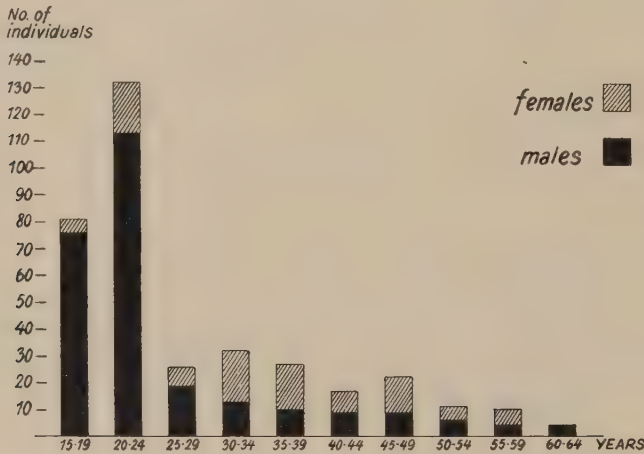


Fig. 2.

Age and sex distribution in the material (263 males, 99 females).

On plotting the results graphically I have obtained a deeply indented curve whose downward points all correspond to values to half millimetres. This is a familiar psychological phenomenon, due to the fact that Hertel's apparatus does not permit of readings to a greater accuracy than $\frac{1}{2}$ mm. The same phenomenon is to be found in Lee's material.

In order to obtain a distribution curve capable of providing a better illustration, I have distributed the numbers of these Hertel measures to $\frac{1}{2}$ mm. equally to both of the nearest groups. The result appears from Fig. 3, which shows quite a regular, ascending part of the curve; the peak corresponds to 17 mm., then a bend at 18 mm., a steep fall to 19 mm., followed

by a gradual fall. The curve for males is fairly congruent with the general curve, whereas that for females is not peaked, but has an approximately horizontal plateau corresponding to 16-18 mm. with the highest point at 18 mm., or somewhat to the right of the male peak and corresponding to the afore-mentioned bend on its descending part.

A cumulative frequency curve plotted on the basis of the original values (including Hertel measures to $\frac{1}{2}$ mm.) described

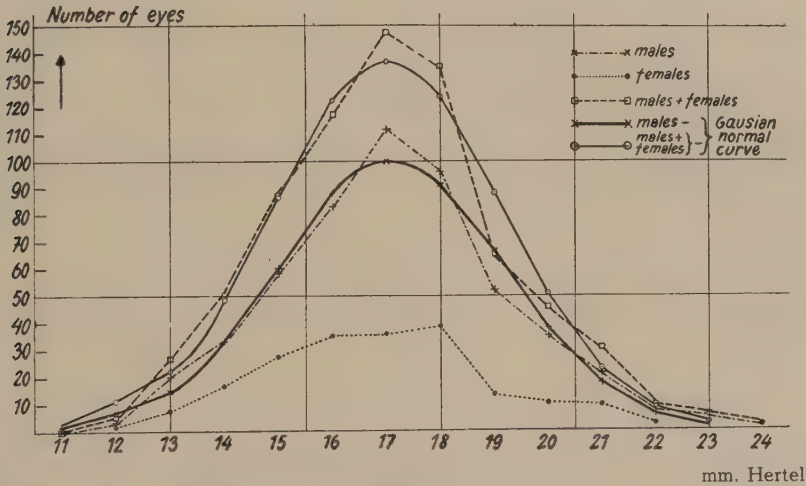


Fig. 3.
Hertel measures. Distribution curves.

a fairly even rise, chiefly between 14 and 19 mm.; a new distribution curve plotted from values from the smoothed-out cumulative frequency curve was found to have a course on the whole like that in Fig. 3, and therefore I shall continue to work with the values of the latter.

The mean for males is 17.1 mm. (526 eyes), for females 16.8 mm. (198 eyes) and for the whole material 17.0 mm. (in all 724 eyes).

Statistical calculations¹ show that the standard deviation is very nearly the same for males and females, 2.08 mm. and

¹ Made with the assistance of Mr. H. T. Stenby, C.E., and Dr. Gerh. Rønne.

2.05 mm. respectively, and for the whole material 2.08 mm. From the standard deviations (SD) we calculate the probable limits of the distributions as shown in the table below:

	No. of eyes	Hertel measure (mean)	SD	95 % within	99 % within	99.9 % within	mm.
Males ...	526	17.10	2,075	13.0-21.2	11.8-22.4	10.3-23.9	"
Females .	198	16.84	2,048	12.8-20.9	11.6-22.1	10.1-23.6	"
M + F ...	724	17.03	2,080	13.0-21.1	11.8-22.4	10.2-23.9	"

As will be seen from Fig. 3, the outer limits for males are 11 mm. and 24 mm., for females 12 mm. and 22 mm., which lie within the calculated probable limits shown above. For additional comparison with the above table I may add that from a distribution curve plotted according to the percentage occurrence in my material the following was found to apply to the total material:

99 %	had Hertel measures between 12.1 and 22.3 mm.
95 %	" " " " 13.4 " 20.7 "
90 %	" " " " 14.6 " 18.9 "

A statistical calculation¹ showed that the difference between the means for males and females is not significant but must be viewed as the result of fortuitous circumstances.

On Fig. 3 I have plotted normal distribution curves (Gaussian), calculated from the means and the standard deviations for the total material and for the males alone. On the whole there is good conformity between the measured and the calculated distribution curves, though the agreement is better for males alone than for the total material, the female material being the more irregular, due presumably to the relatively small number of measurements (198 eyes) on females as compared with the 526 measurements on males.

It will be seen from Fig. 3 that for both of the measured curves the numbers with 17 mm. and 18 mm. are too high and

¹ $t = 1.355$ for $n = 722$ degrees of freedom, i.e. P lies between 10 % and 20 %. Usually, a result is only significant, if $P < 5$ %.

the numbers with 19 and 20 mm. too low. The question whether these divergences were the result of refraction anomalies was gone into, but apparently they were not, as the same phenomenon was found in a distribution curve for 371 emmetropic eyes (male); the cause must therefore be sought elsewhere, perhaps in the age distribution.

As the ends of the curve and its ascending part closely follow the course of the normal curve, it may be taken for granted that among the persons examined there was no abnormal state as regards their orbital anatomy and that there is no systematic error in the measuring technique. The explanation of the wryness of the descending part of the curve (for both males and females) may possibly be as follows: In judging what persons were suitable for soldiers or nurses (these categories forming the greater part of my material), the authorities may perhaps have been too critical and rejected a number of normals with relatively protruding eyes on a suspicion of hyperthyrosis; had these been included in the material, the curve might have been somewhat higher and its descending part pushed a little to the right (and thus have coincided better with the normal curve). If this hypothesis is correct, it means that there is less latent hyperthyrosis in the population than is generally assumed. The other explanation may be that among the persons examined there is a latent hypothyrosis with relatively low Hertel measures, so that the wryness in the curve may be imagined as being the result of too few with values of 18.5-20 mm., and on the other hand too many with 17-18 mm.

However, the deviation from the normal distribution is not of statistical significance, as the Chi-square test shows¹. Accordingly, *both measured distributions* (Fig. 3: males + females and males alone) *agree well with the Gaussian distribution*

¹ χ^2 test for males and females gives: $\chi^2 = 16.18$ with 8 degrees of freedom, which corresponds to $P = 4.2\%$; for males alone $\chi^2 = 7.09$ with 7 degrees of freedom, corresponding to $P = 43\%$. It is generally reckoned that when $P > 1\%$, there is no real disagreement between theory and observation.

curve, and the deviations are fully explainable by fortuitous circumstances.

On dividing the material into three age groups, as in the following table, we arrive at the following means for the Hertel measures (the number of eyes shown in brackets):

	15-19 years	20-29 years	30-64 years
Males	16.71 mm. (152)	17.15 mm. (264)	17.50 mm. (110)
Females	16.30 mm. (10)	16.72 mm. (54)	16.81 mm. (134)
M + F	16.75 mm. (162)	17.04 mm. (318)	16.79 mm. (244)

It will be seen from this table that the Hertel measures increase slightly with age, rather more for males than for females. The middle age group is best represented (318 eyes), with the result that it sets its impress on the general curve; it is within this group of young people that values between 14 and 19 mm. occur with relative frequency. In the oldest age group there are proportionately more higher values, which may perhaps be connected with the more frequent adiposity among individuals of over 30 years and hence increased orbital fat.

The relatively high average values shown by my material compared with those of other authors (see Fig. 1) may perhaps have their explanation in a latent hyperthyrosis in the population. According to an investigation by *K. Iversen*, hyperthyroidism is manifested mainly between the ages of 30 and 50. This being so, latent hyperthyroidism must presumably be sought chiefly in the third decade, to which two thirds of my subjects in fact belong. As hyperthyroidism occurs mostly in females, I decided to compare the Hertel values for females between 20 and 35 years with the values for the other females (15-19 years and 35-64 years). The two groups are of about equal size. The mean value for the former group (104 eyes) is found to be 16.55 mm., for the latter (92 eyes) 17.0 mm. Thus these curves do not suggest latent hyperthyrosis with increased Hertel measures in the young. A material in which the various age groups were somewhat more equally represented would be more suitable for elucidating this question.

The conclusion to be drawn from my investigations must be that Hertel measures of 20.5-21 mm. should be regarded as highly suspect if there is no excessive myopia; values of 22 mm. or more must usually be reckoned as pathological. If the examined eye is hypermetropically shortened, the limit of course must be placed lower. For the rest, in diagnosing exophthalmus one's deliberations must in each case include the patient's own statements—and especially those of his family—as to his appearance supported if possible by earlier photographs of him.

The relative Hertel measures in my material will appear from the following table:

Difference in Hertel measures mm.	Number of individuals		Total	%
	R. eye protruding more	L. eye protruding more		
0			159	44
0.5	39	31	70	19.7
1.0	79	42	121	33.4
1.5	8	0	8	2.2
2.0	3	0	3	
2.5	1	0	1	
	130 (36 %)	73 (20 %)	362	

Of the 362 individuals examined, 159 had unequal measures for the two eyes, whereas in 203 (56 %) there was a difference varying between 0.5 and 2.5 mm., though it was in very few cases that the difference exceeded 1.5 mm. and in 94 % of them it was not in excess of 1 mm. These figures agree very well with those found by *Schlabs*; but whereas that author found that the right eye had the largest measure in every case, my figures show that barely two-thirds had the higher value for the right eye. Most other authors also find the right eye more protruding in most cases.

As I said before, in most cases I also recorded the distance between the external orbital margins. The result is given in

Fig. 4: in 250 individuals there were values ranging between 89 mm. and 107 mm., average 97 mm., and, as might be expected, rather higher for males, 97.5 mm. (207 measurements) than for females 94.4 mm. (43 measurements). *Schlabs* in his material found the distance to vary between 91 mm. and 106 mm., *Lee* between 87 and 110 mm. *Emmert* found an average of 99.7 for

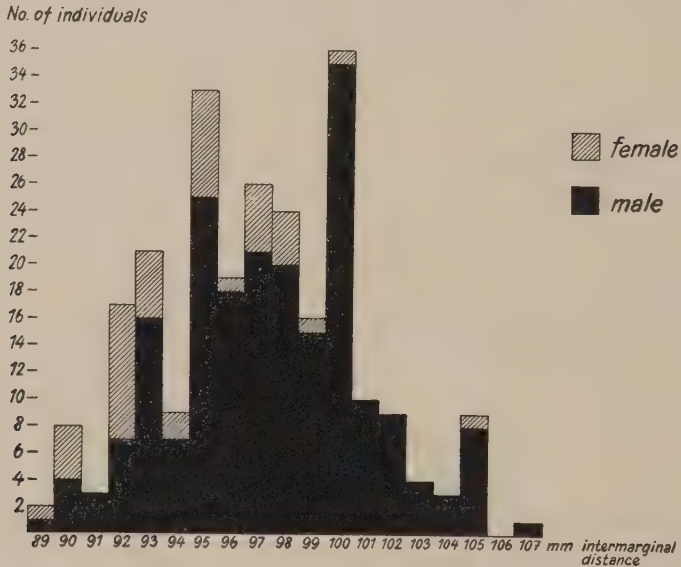


Fig. 4.

Distance between external orbital margins in 270 individuals (207 males, 43 females).

males and 96 mm. for females. Fig. 4 also shows the result of a psychological phenomenon, there being relatively many with values of 90, 95, 100, and 105 mm., corresponding to the fact that on the millimetre scale of the Hertel apparatus these values are indicated by figures. In 1906 *Wolff* measured the skulls of many different human races; on the skulls of 73 Swiss the "biorbital breadth" was found to vary between 90 mm. and 105 mm., averaging 97.4 mm.

The practical advantage to be derived from the results of my investigations will be partly in the evaluation of absolute Hertel measures and partly in the judging of unequal measures

in a patient. What the various authors consider to be the range of normal values and the average values differs somewhat, presumably on account of the different qualities of the human materials examined as regards race, age, and sex. Most are agreed that it is impossible to lay down sharply defined limits for what is to be considered the normal, and so they merely give average values. For instance, *Ehlers* and *Behrens & Zuckerman* give an average of 12-14 mm. *Kestenbaum* maintains that the normal values are between 12 and 17 mm. and that values outside this range are pathological. But most ophthalmological textbooks and manuals refrain from giving any normal values at all. It may roughly be reckoned, as pointed out by *Cohn* and *Kestenbaum*, that the vertex of the cornea should normally lie more or less in a frontal plane through the superior orbital margin and the inferior orbital margin.

My results give perceptibly higher normal values than those of earlier authors. Of the latter (Fig. 1), *Helmbold's* are closest to mine, with averages of 16.67 mm. for males, 15.68 mm. for females (17.1 mm. and 16.8 mm. in my material). The range of my measures extends right from 11 mm. to 24 mm., it is true, but only 5 % have values below 13.4 mm. and higher than 20.7 mm. The average values are round about 17 mm., slightly lower for females than for males, i.e. much higher than what other investigators have found. It should be borne in mind, however, that most have employed another measuring apparatus, not nearly so many subjects and a less homogeneous human material, for children, very old people, and persons with pathological eyes, e.g. pronounced refraction anomalies, are included. For this reason a direct comparison will give no useful result.

When the two eyes have different degrees of protrusion the diagnosis of exophthalmus will not cause much difficulty, if only the difference is well marked and there is no facial asymmetry. If the difference is one of only a few millimetres, it will often be hard to decide whether it is due to slight and unnoticeable cranial asymmetry, an experimental error, or to a slight

unilateral exophthalmus. As will be seen from Fig. 1, most authors have found a greater or smaller difference in the degree of protrusion in many normal individuals—some up to 2 or 3 mm. Measured with Hertel's apparatus, however, the difference did not exceed 1.5 mm. *Ehlers* states that a difference of 1 mm. must be regarded as a suspicious sign of unilateral exophthalmus; this is confirmed by the results of my investigations, as in my 203 cases of unequal Hertel measures only 6 per cent. had a difference of over 1 mm. Naturally, in unilateral exophthalmus one must also take the anamnestic information into consideration.

To summarize, it may be said that whenever there is a suspicion of exophthalmus a good many factors must be taken into consideration, such as history, race, sex, age, physical type, stature, state of nutrition, cranial form, refraction, etc., and the exophthalmometer measurements must be evaluated in the light of these factors, combined with our knowledge of the values for normal individuals. I hope that the present investigations will be found capable of contributing towards that knowledge.

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Les lésions embryonnaires, à la lumière des défauts mammaire et pectorale, de la syndactylie et de la microdactylie

Par

KNUD H. KRABBE

En étudiant les anomalies congénitales l'attention des savants s'est portée le plus souvent sur les éléments héréditaires, surtout sur la perte des gènes. On peut prendre comme exemples l'achondroplasie ou le mongolisme.

Au cours de ces dernières années, on a commencé à s'intéresser aux facteurs exogènes comme pouvant être la cause de défauts congénitaux — par exemple, la rougeole pendant la grossesse causant des anomalies chez les nouveaux-nés, l'influence des facteurs Rh., ou ce que l'on a connu pendant longtemps, déjà, l'amputation des extrémités par des cordons d'amnion. Toutes ces influences doivent être considérées comme exogènes par rapport au développement des embryons.

J'ai eu l'occasion d'observer un cas qui me semble fournir quelques éclaircissements sur l'origine des défauts congénitaux d'une nature spéciale.

Il s'agit d'une femme, âgée de 37 ans admise en novembre 1947 au Service Neurologique de Kommunehospital à Copenhague par suite de douleurs dans le dos. Ces douleurs étaient probablement causées par des myoses dans les muscles dorsaux. Il ne faut pas analyser son histoire en ce qui concerne cette maladie, assez banale et sans intérêt spécial. Ce qui était intéressant dans ce cas, c'était une dysplasie de l'extrémité supérieure droite et de la partie thoracique droite.

Il n'y avait aucune disposition familiale.

La dysplasie était congénitale et stationnaire, en ce qui concerne l'extrémité droite et le muscle pectoral. A l'époque de la puberté, la glande mammaire gauche se développa normalement, tandis que la glande mammaire droite ne se développa pas du tout.

L'examen objectif montra ce qui suit :

Dans l'extrémité supérieure droite, le bras était de la même longueur et du même volume que celui de l'extrémité supérieure gauche. L'avant-bras était un peu hypoplastique, la main encore plus. Il y avait une membrane interdigitale le long de la phalange (proximale) entre les doigts II et III. De même entre la moitié proximale de la phalange des doigts III et IV, et IV et V.



Fig. 1.

Tandis que la phalange semblait très peu raccourcie, la phalangine et la phalangette des doigts II, III et IV paraissaient très raccourcies (Fig. 1—2). De plus, l'articulation distale de ces doigts avait un aspect ankylotique.

Ceci était dû, comme les radiogrammes l'ont démontré plus tard, au fait que la phalangine manquait, ou, si on veut, que la phalangine et la phalangette des doigts II—IV étaient fusionnées en une pièce. Au doigt V, la phalangine et la phalangette étaient séparées, mais fortement raccourcies. Le pouce était normal. Les ongles étaient normaux, pas diminués.

L'omoplate droite était de même volume que l'omoplate gauche, mais il y avait omoplate ailée à quelque degré du côté droit.

Tandis que le bras était tout à fait normal, le thorax présentait une anomalie frappante. Le sein droit manquait totalement, de même que la mamelle (Fig. 3). Du côté gauche, le sein était bien développé. De plus, les muscles pectoraux majeur et mineur n'existaient pas. Correspondant à ces déféctuosités du sein et des muscles pectoraux, il y avait aussi une déféctuosité des côtes III et IV. Un fragment de 5 cm. environ de longueur manquait à chaque côte. Toute la partie postérieure et latérale était conservée ainsi qu'une petite partie sternale, aiguë, de 3 cm. environ de longueur. Les autres côtes et les clavicules étaient normales.

Quand la malade pressait, on observait sur la peau une proéminence de 5×5 cm. correspondant à la défectuosité des côtes.

Du côté gauche, le thorax était normal, la côte III étant seulement un peu surélevée dans la partie parasternale.

L'examen radiographique fournit les indications suivantes : Le squelette de la main droite était aplastique par comparaison avec celui de la main gauche. Les phalanges des 4 doigts cubitaux manquaient ou étaient très peu développées. Les parties molles présentaient les mêmes caractéristiques que celles que l'on pouvait observer directement : syndactylie partielle entre les 4 doigts cubitaux, plus marquée entre les II^e et III^e doigts (Fig. 4).



Fig. 2.

La radiographie du thorax montra correspondant à l'aplasie palpable, des défectuosités des côtes III et IV (Fig. 5). La radiographie de la colonne vertébrale ne donna rien d'anormal dans les os ou les articulations. Les espaces intervertébraux étaient de hauteur et de délimitation normales.

En résumé, les anomalies constatées chez cette malade, se présentent comme suit : A la main droite, syndactylie partielle et aplasie des phalanges des doigts II, III et IV, raccourcissement de la phalange et de la phalangette du doigt V, tandis que le pouce était normal. De plus, aplasie totale du sein droit, de la mamelle droite et des muscles pectoraux droits. Enfin, défectuosité dans la partie antérieure des côtes III et IV du côté droit. Mais les parties intermédiaires, le bras et l'épaule, étaient normales, pas aplastiques.

Il y a donc, chez la malade des défectuosités dans deux parties séparées du corps. Comment expliquer ces anomalies ?

En premier lieu, on peut relever que ces anomalies ont leur origine dans le deuxième mois de la vie embryonnaire, où les doigts ne sont pas encore séparés. Une syndactylie secondaire peut être considérée comme exclue.

Si l'on considère un embryon humain de cet âge, on voit que la longueur de l'extrémité supérieure permet juste à la main de couvrir la partie mamellaire lorsque l'extrémité est élevée et antéro-posée. C'est dire qu'une pression extérieure peut en même temps presser la main et la partie mammaire sans léser l'épaule. C'est en effet l'explication la plus naturelle et la plus vraisemblable.

La question qui se pose ensuite est celle de savoir quelle influence peut produire cette pression sur la main et la poitrine.

A une phase si précoce il n'est pas probable que des fibromyomes de l'utérus puissent se traduire par une pression si limitée sur la poitrine. Il faut se souvenir qu'il s'agit d'une étendue de quelques millimètres. Il est très peu probable également

que des cordons d'amnion qui peuvent provoquer des amputations des membres, puissent causer une pression si localisée.

Pour approfondir le problème de la cause de la pression, il faut jeter un coup d'oeil sur la littérature. Nous avons réussi à trouver 50 cas environ donnant la description de cette combinaison singulière : Syndactylie et défectuosité pectorale unilatérale.

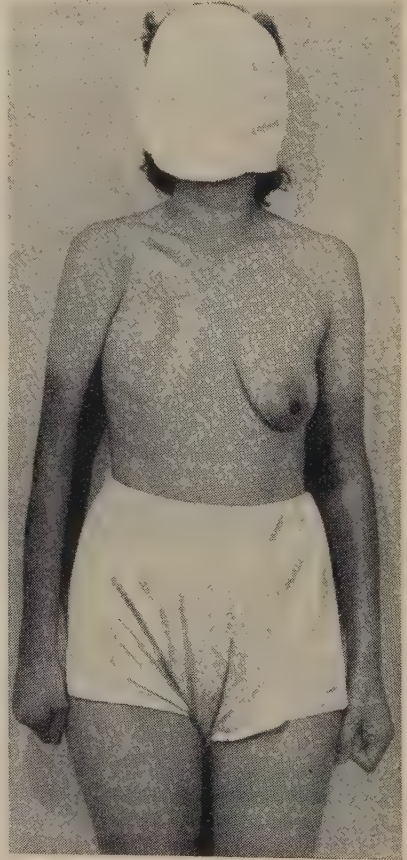


Fig. 3.

Le premier cas décrit semble être celui de *Poland* de 1841, le dernier celui de *Resnick* de 1942. Un travail qui décrit cette anomalie d'une manière très détaillée est l'œuvre de *Robert Bing* de 1902. La seule description scandinave que je connais est celle de *C. M. Furst* de 1900.

De plus, on trouve dans la littérature un très grand nombre de communications sur l'absence du muscle pectoral unilatéral

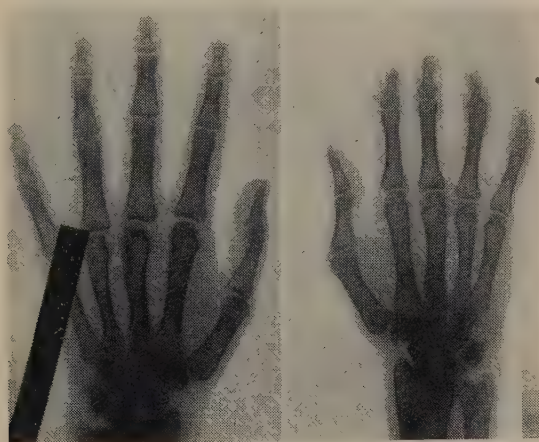


Fig. 4.

— un nombre si élevé qu'on juge que plus de 90 % des défectuosités musculaires congénitales sont des aplasies unilatérales des muscles pectoraux.

Comment expliquer ce grand nombre d'aplasies pectorales unilatérales ?

La seule réponse plausible semble être : le menton.

En regardant un embryon du second mois de la vie fœtale, on constate que si la tête est courbée en avant, le menton se trouvera justement pressé vers la partie de la poitrine où sont les muscles pectoraux et où se trouve de plus, la main encore syndactylique si le bras est placé en avant.

On sait qu'il existe des cas où la quantité de liquide amniotique est très diminuée. Il est probable que c'est justement dans ces cas

que la tête est inclinée en avant de sorte que le menton est pressé vers la poitrine.

On peut alors se demander : Mais, dans ces cas, pourquoi ne trouve-t-on pas de défauts du menton ?

En effet, il y a dans la littérature des descriptions de cas où l'on trouve, outre la syndactylie et l'aplasie pectorale, une

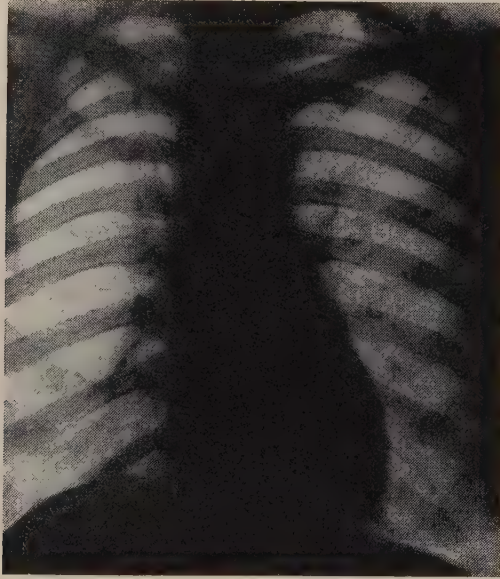


Fig. 5.

empreinte au menton. Et il est probable qu'il existe beaucoup plus de cas de ce genre où une petite empreinte sur le menton a échappé à l'observation. Enfin, il est possible que dans cette phase, le menton ait une résistance plus grande que les muscles pectoraux.

Naturellement, ces considérations sont purement théoriques. Mais il faut se demander s'il y a une autre explication plus vraisemblable ?

En parcourant la littérature, j'ai trouvé un auteur, le premier, ayant avancé la même théorie en ce qui concerne l'explication du fait que la syndactylie est assez souvent combinée à l'aplasie

pectorale. C'est *Johannes Schoedel* qui écrit en 1902 : que ces dysplasies combinées doivent être dues à une pression sur la main et la poitrine dans une phase de la vie embryonnaire où la main est située devant la poitrine.

Si cette théorie est justifiée, il faut se demander si elle peut être étendue à d'autres anomalies congénitales.

Tout d'abord, comme mentionné plus haut, il nous semble le plus vraisemblable que les défectuosités des muscles pectoraux, relativement si communes, sont causées par une pression du menton. Mais il est possible aussi que des cas de syndactylie sans aplasie pectorale puissent être produits par pression du menton sur la main, cette pression n'étant toutefois pas assez forte pour produire une aplasie pectorale. De plus, il faut se demander si les cas congénitaux de poitrine en entonnoir peuvent se produire par une pression du menton, non latéralisée comme dans les aplasies des muscles pectoraux, mais par pression en ligne médiale.

Enfin, il faut examiner la question de savoir si l'origine de l'acrocéphalosyndactylie est due à une diminution du liquide amniotique à une époque précoce de la vie embryonnaire, dans le second mois de la grossesse.

Il est bien connu que l'acrocéphalosyndactylie se trouve quelquefois chez plusieurs frères et sœurs. On a considéré alors la maladie comme héréditaire. Mais il faut envisager que cette maladie, ou plus correctement cette anomalie, n'est pas héréditaire au même sens que par exemple les myopathies progressives ou la chorée de Huntington. Ce qui conditionne l'anomalie congénitale peut aussi bien être une anomalie de l'utérus maternel faisant qu'il y a trop peu de liquide amniotique dans plusieurs grossesses.

En tout cas, l'existence de l'aplasie pectorale combinée de syndactylie et de microdacylie indique, que dans les cas de syndactylie il faut examiner s'il y a aussi de légères modifications de la poitrine et de la mandibule.

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Metastatic Abscess of the Brain- Surgical Treatment and Results

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I.

This study is limited to the brain abscesses we treated with the help of *penicillin*, from November 1944 to March 1949. Firstly, table 1 shows the general incidence of metastatic brain abscesses: 18 were found out of a total of 55 cases, the proportion being about one third of all brain abscesses, and this in spite of the large number of traumatic abscesses following war wounds in 1945-46. Let us remark that 15 meningeal abscesses (none of them metastatic), with 6 deaths, were found during these four years and a half, making a general total of 70 cases of intracranially localised suppurations. As to mortality, it is seen in table 1 that mastoid-born abscesses were very severe, surprisingly enough. In fact most abscesses belonging to this class are successfully treated by the ear specialists and only or nearly only complicated cases are sent to the neurosurgeon—at least in Paris.

TABLE 1.
Aetiology and Mortality of 55 Cases of Brain Abscess.

	No. of cases	Died
Metastatic Infections	18	6
Cranio-cerebral Injuries	17	3
Mastoid Infection	9	4
Meningitis	4	0
Sinus and Face Infections	2	1
Unknown	5	3
	55	17 (31 %)

In the other groups, metastatic abscesses show the highest mortality with the possible exception of the group labelled "origin unknown" in which we are fairly certain that a good number are in fact metastatic. But it was decided to study in details only the 18 cases the origin of which is undoubtedly metastatic.

When it is remembered that before the penicillin era the mortality of this group was above 95 %, the advance now realised is seen at once, since mortality fell to 33 %. This is in accordance with recent publications on the subject of metastatic and singularly thoracogenic abscesses (3, 5, 6). But an analysis of our metastatic cases will, it is hoped, lead to some useful data on their surgical treatment (Table 2).

TABLE 2.
Analysis of 18 Cases of Metastatic Abscess.
(Number of deaths are in brackets).

<i>Aetiology</i>		<i>Bacteriology</i>		<i>Location</i>	
Lung	11 (4)	Streptoc.	5 (3)	Occipital	9 (2)
Heart	2 (1)	Staphyl.	6	Parieto-	
Carbuncles	3	Pneumoc.	2	Rolandic	5 (3)
Uterus	1	Anaerobic	1 (1)	Fronto-	
Tooth	1 (1)	Multiple	2 (1)	Temporal	3
		No germs found	2 (1)	Cerebellar	1 (1)
<i>Anatomical type</i>		<i>Evolutive type</i>		<i>Surgical Treatment</i>	
Multilocular	12 (3)	Acute	8 (4)	Complete	
Single	6 (3)	Chronic	10 (2)	excision	13 (2)
				Other methods	5 (4)

Aetiology: Pulmonary and pleuropulmonary infections come first, being responsible here for about two thirds of our 18 cases; their death rate (35 %) is roughly the same as for the whole group of metastatic abscesses. Nevertheless, it should be noticed that 3 abscesses secondary to skin infection (carbuncles) were all cured in spite of the fact that 2 of them belonged to the acute form:

this relative benignity has apparently something to do with the germs (staphylococci). Whatever the aetiology is, nearly all our cases occurred in *male* patients (16 out of 18).

Bacteriology: The special severity of streptococcic abscesses is evident at once, since 3 out of 5 died. Among these 5, three were acute. All of them were secondary to lung infection. On the other hand, staphylococcic abscesses are relatively benign, since our 6 cases were all cured, including 2 acute cases and 2 in which the brain abscess was associated with a meningeal sup-pururation (1 subdural, 1 extradural).

Location: The marked predominance of metastatic abscesses in the posterior half of the brain is striking in our series since 14 out of 18 belong to this location. This corresponds to the territory of the postero-superior groups of the Sylvian collaterals. As usual, in our thoracogenic cases, the brain abscess was on the same side as the lung lesion, which, according to some authors, favours the theory of venous rather than arterial embolism (6). If we leave aside pathogenic considerations to discuss only the location, our findings are not in accordance with those of Rizzoli, McCune and Sherman, who observed at least half of their metastatic abscesses in the frontal lobes, but this concerns only the *cured* cases, since the authors do not tell how many fatal cases were observed. In Pennybacker and Holmes Sellors' article, 12 abscesses were "fronto-parietal", and only 4 "temporal". The predominantly parieto-occipital location of metastatic brain abscesses impressed us so much that it would be interesting to check it on larger numbers.

Anatomical type: Multilocular abscess is by far the more common type (two thirds) and, as will be seen below, this anatomical fact is the strongest point in favour of our method of total excision as opposed to aspiration methods (3, 4). We did

not see multiple abscesses in this group. Multilocularity was frequently observed by the Oxford surgeons (5), perhaps less frequently by the Washington surgeons (6). Multilocularity always goes with an irregular capsule, especially thin closest to the ventricle.

Evolutionary type: We observed nearly as many acute abscesses as chronic ones, the death rate being twice as high among the acute cases, as could be easily foreseen. The special severity of acute abscesses mostly comes from spreading brain oedema, and this is the main reason which leads us to advocate in acute cases the excision of the abscess and of some surrounding oedematous white matter.

By acute abscess we mean a young abscess with usually little pus and much brain oedema. The question of the capsule is perhaps less significant, since even in ten days encapsulation can be definite enough, but it is irregular, absent in places, and surrounding brain oedema is predominant. This early encapsulation might depend on systemic treatment by penicillin, so often used now in lung or other infections.

II.

Before discussing the surgical treatment of metastatic brain abscesses, a detailed case report will be given, as fairly typical of our present method:

Case report. Acute multilocular abscess in right occipital lobe, metastatic from a chronic suppuration of the lower lobe of the right lung. Complete excision of brain abscess (piecemeal)—Recovery.

Cab...., 45 years old, in the first days of January and in the third week of the same month exhibits some temperature (38.5) with cough and "cold in the nose". A few days later, he complains of occipital headache and feels slightly sick and dizzy. During the first week of February vision is at times blurred by luminous spots and rays for several hours in succession. These symptoms disappear when on February 8th, the patient himself notices that he cannot see in the left half of the visual fields. Headaches get worse and permanent. At the same time some slowness of thought and tendency to

sleep during the day are observed. No papilloedema and no other neurological disturbances.

When the patient is seen on February 15th, he is fairly cooperative and tells of an acute lung infection in 1944-45; since that time he complains of "bronchitis" every winter. Neurological examination shows at once a left hemiplegia which has existed since the previous evening.—One day later, consciousness is blurred; the left hemiplegia is massive with brisk reflexes (the same on both sides) and plantar flexion. On February 17th, the patient is nearly unconscious, with stiffness of neck, the head being rotated to the left. It is painful to try to rotate it to the right, and pressure on temporal fossae is definitely painful on the right side.

Diagnosis: acute metastatic abscess of the right side of the brain, occipital, or posterior temporal.

Penicillin (500,000 U per 24 hours) is instituted. A blood therapy count showed 4,450,000 red cells and 17,500 white cells with 90 % polys.

17-2-49. Through a right temporo-occipital burr-hole the abscess is found, 3 cms deep. Foul and thick pus. 100,000 penicillin units and 4 cc diodrast are injected into the abscess. X-rays show an anterior right occipital abscess, medially situated (calcarine fissure); the irregular picture is the visual proof of a multilocular abscess. In spite of penicillin therapy and intravenous injection of 120 cc hypertonic SO₄Mg, no improvement.

18-2-29 *complete excision, piecemeal, of multilocular abscess.* Occipital osteoplastic flap. After opening the dura, the abscess is seen in the medial half of the occipital lobe; it reaches the cortex along the falx. The abscess is deliberately opened up and aspirated with a double effect aiming at lessening normal brain damage: (1) its volume is reduced; (2) the excision is now possible from the inside. It is a typical multilocular case with a marked irregularity in the capsule: in some places the walls are very thick but still soft, fibrinous; in others they are nonexistent, especially nearest the ventricle which is opened wide. Finally complete excisions is achieved, which means excision not only of the definite capsule but of some surrounding oedematous and thickened white matter. The anterior and medial fourths of the occipital lobe are destroyed by the abscess, which was centred on the calcarine fissure. Gelatin-thrombin is placed into the cerebral cavity; 20,000 penicillin units are instilled into it, plus 20,000 into the ventricle. The dura is completely closed; the flap is replaced, covered with a paste of 50,000 penicillin units and 3 grams sulfanilamide. The skin is stitched in the usual two layers without drainage.

No germs found in the abscess, but pus aspirated before local instillation of penicillin was not examined at once.

Evolution: For ten days 500,000 units of penicillin were given daily, 50,000 units by spinal taps for five days, and 50,000 units daily into the operative wound for 6 days. Improvement was

immediate and more marked every day. Temperature never reached 38.5. The left hemiplegia subsided in a month, leaving weakness and superficial hypesthesia (no astereognosis). But the left homonymous hemianopia persists unchanged.

The X-rays of the lungs show a dense focus with bronchiectasis limited to the lowest right lobe; surgical excisions is decided on in May, when the general condition of the patient, though good now (April 5th), will be even better after a rest in the country.

III.

SURGICAL TREATMENT

Our method is an extension to all kinds of abscess of Clovis Vincent's method (7) (complete extirpation of chronic encapsulated abscess). Now, with penicillin, post operative meningitis does not exist any more, *if the excision is complete*, even after wide opening up of the abscess and the ventricle. This complete extirpation piecemeal if necessary, was described at length in 1945 in Paris, and later (3, 4). Nowhere does it seem more useful than in metastatic abscesses which, as a rule, are multilocular; therefore to rely only on aspiration methods in these cases seems hazardous. We believe in radical extirpation of metastatic abscesses not only in the *chronic* but in the *acute* stage as well. An acute abscess threatens life mostly from brain oedema and temporal herniation.

Aspiration and decompression in our experience are inadequate to cope with the danger of acute temporal herniation, even with the help of penicillin. Brain oedema, which is sometimes immense in acute abscesses, is inflammatory first, but, in our opinion, gets more and more marked when temporal herniation and pressure on the brain stem are installed. At this stage something more than penicillin and aspiration is usually required to relieve the brain stem, and we believe this to be excision of the abscess through a bone-flap. Another factor may intervene in the production of spreading brain oedema: the pressure on

the rolandic veins, and this may account for the special severity of our parieto-rolandic cases.

Reasons to adopt complete excision in nearly all cases as the standard method against metastatic abscesses come under three headings: death-rate, neurological sequelae, length of stay in hospital.

DEATH RATE AND CAUSES

6 fatal cases were observed: 2 after complete extirpation (out of 13 cases (15 %)); 4 after other methods (out of 5 cases (80 %)). Obvious as the advantage of excision looks, it is worth while analysing the causes of deaths.

(1) Complete excision. Patient comatose; single acute right rolandic abscess after malignant endocarditis.—Anaerobic organisms found in cerebral abscess.—Death due to brain oedema. In this case it may be argued that aspiration and intensive penicillin therapy (which was of course used) would have been a better procedure. We believe the patient's condition was too serious anyway.

(2) Complete excision. Acute right multilocular rolandic abscess, from lung infection. Streptococci. Death by brain oedema.

(3) Decompressive flap and aspiration. Acute multilocular left rolandic abscess, from lung infection. Death by temporal herniation.

(4) Incomplete excision (personal case). Patient semi-comatose; single cerebellar abscess involving the vermis and definitely pressing on the pons. Origin: teeth infection; cocci and bacilli gram + found in cerebral abscess. Death due to brain stem disturbance. Aspiration might have yielded better results, so close to the brain stem was the abscess.

(5) Partial excision.—Chronic multilocular left occipito-temporal abscess, from lung infection.—The ventricle was opened and a definite part of the abscess left in place. Death followed streptococcic meningitis, not unexpectedly.

(6) Intraventricular penicillin. Acute juxtaventricular right occipital abscess, from lung infection. The abscess was missed; the patient was treated only for streptococcic meningitis, responsible for death.

The following comments seem logical:

(a) In Cases 4,5, and 6, death is due to possibly avoidable mistakes: excision to succeed should be complete (Cases 5 and 6) and it is probably futile to try it when the abscess is too close to the brain stem (Case 4).

(b) Case 1 does not mean much, the patient's condition being too critical.

(c) Cases 2 and 3 are interesting to compare, since they were anatomically similar. We firmly believe in the advantage of complete excision over aspiration methods, which can only be misleading in the case of a multilocular abscess. Nevertheless, it must be agreed that the treatment of acute multilocular streptococcic rolandic abscesses is still exceedingly difficult: brain oedema must be reduced at all costs, and the surgical procedure is liable to exaggerate it by sheer traumatism.

To sum up: we have reason to choose complete excision as soon as possible in the treatment of metastatic brain abscesses, from the point of view of mortality with the following two possible exceptions:

Abscess close to or in the brain stem, as discussed by Cairns (1).

Acute parieto-rolandic abscess, where aspiration can be tried first, but not for too long, as temporal herniation with quick death is apt to develop in a few hours.

It seems to us that the English authors (5) do not rely on pre-excision aspirations either, except when the patient's condition is very poor; complete excision is definitely their aim, as soon as they judge it possible.—This question of when to perform radical extirpation of an acute abscess is certainly still ticklish:

it should be remembered that, as far back as 1936, J. King performed it successfully, and in a personal letter written 3 years ago Dr. Eduard Busch told me he too did it several times. I believe that the early excision of an acute brain abscess will be performed more and more often (in the present state of chemotherapy).

NEUROLOGICAL SEQUELAE

Aspirations methods, especially when drainage is used, are much more likely than extirpation to leave a large scar with subsequent development of epilepsy. Clean excision is of course a much better procedure and the sooner it is done, the better.

But there is another point, very well set forth by Pennybacker (5). Extirpation of a single encapsulated abscess gives a minimum neurological disturbance, even in the rolandic zone. Piecemeal complete excision of a multilocular abscess, especially if it is an acute, ill-defined one, is much more liable to destroy forever important parts of the brain. This is only partly true: the main feature of our method of dealing with a multilocular abscess is *the deliberate opening up of the abscess and its extirpation mostly from the inside*. One excises the abscess as one should excise a deep-seated large-sized meningioma; of course the more acute the abscess is, the more delicate is the operation.

In the case report published here, the patient had two main neurological disorders: left hemianopia, 3 weeks old, and left hemiplegia, 3 days old. The hemiplegia subsided quickly enough (if not yet completely), but the hemianopia is unchanged. The abscess being centred on the calcarine fissure, we believe the optic radiations were destroyed by the abscess itself and not by the operation.

Generally speaking, up to now, we do not see, in our surviving patients, more neurological sequelae than in the prewar ones. But this comparison is only fair for chronic cases, so few were the acute cases who survived before the penicillin era.

LENGTH OF STAY IN HOSPITAL

This third point is less important than the preceding ones. Nevertheless it should be emphasized once more that, with the complete excision method, without drainage, the patient rarely stays in the hospital more than 2 or 3 weeks. It is far more gratifying for the surgeon and for the patient's family than the aspiration and drainage methods.

In this respect we differ, at least partly, from the conclusion of Rizzoli, McCune, and Sherman (6): they report 10 cured cases, 3 by aspiration, 4 by enucleation after drainage, 2 by immediate enucleation, 1 (suspected) by chemotherapy alone. It is not clear whether the authors had fatal cases at the same time, and it would be very interesting to know how and after what procedure death supervened, if any. Length of stay in hospital was months in some cases, and one cannot help feeling that complete cure could have been achieved more quickly by earlier complete excision. Anyway those results are very gratifying, and, as the authors say, show very vividly how the prognosis of metastatic brain abscesses has changed since the introduction of penicillin.

IV.

CONCLUSIONS

In accordance with our radical extirpation method for all kinds of brain abscesses (4), we advise the following approach in the treatment of metastatic brain abscesses due to penicillin sensitive organisms:

(1) Usually the abscess is suspected when cerebral focal symptoms (such as hemiparesis) and intracranial pressure symptoms (such as headache) appear during a chronic or subacute lung infection. Sometimes the start of the abscess is masked by an acute meningitis. If the first spinal tap shows no organisms, a brain abscess is probable. When organisms are present in the c.s.f., an abscess must be looked for if there is no improvement after intrathecal penicillin therapy.

(2) To find the abscess, the brain is tapped through a burr-hole, the situation of which depends on the neurological signs. Usually a posterior temporal burr-hole will show the abscess. Penicillin (20 to 50,000 units) is instilled after aspiration. Injection of a contrast medium gives beautiful X-ray pictures, but adds scanty information: it does not necessarily show all the loculations.

(3) Ventriculography is not to be advised, especially in the acute stage, where it increases the already threatening brain oedema. But it is useful to show an abscess during a metastatic subacute meningitis, or as a complete cure test in some cases with sequelae.

(4) When the abscess is found, tapped, and filled with penicillin, systemic administration of penicillin (200,000 to 400,000 units daily) should go on for about a week—or more if the lung infection is not quiescent.

(5) If the abscess is a definite chronic one, we always turn an osteoplastic flap and excise it completely in the same session, without drainage. According to the chances of infection (abscess or/and ventricle opened up), 20 to 50,000 units of penicillin are instilled locally and by spinal taps for 4 or 5 days. Sometimes spinal taps are unnecessary.

(6) If the abscess is an acute one, we wait for 24 hours to see the action of aspiration and penicillin. It is only in case of a *dramatic improvement* that we should go on with this method until complete excision days or weeks later. In our experience this is exceptional and improvement was in practically all cases slight or nonexistent. This is why *no later than the following day* we turn a flap and excise the abscess completely; penicillin is given as in chronic cases.

(7) When the brain abscess is cured, primary infection should not be forgotten and this means usually surgical attack on a lung infected focus (Pennybacker (5)): it is the best way to prevent the development of a new abscess in another part of the brain.

To conclude we can do no better than to quote the following

lines by Cairns (1): "We have thus reached a stage in the treatment of brain abscess where the method of complete extirpation, which we owe to the classic work of Professor Clovis Vincent, has become standard for all varieties of brain abscess, with the exception of acute abscess after missile wound of the brain, and the rare chronic abscess which is deep-seated and better treated by repeated aspiration".

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A Surgical Procedure for Atresia of the Aqueduct of Sylvius

By

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INTRODUCTION

The treatment of atresia and stenosis of the aqueduct of Sylvius is a difficult neurosurgical problem. Though the lesion is anatomically small and insignificant, attempts to relieve the resulting hydrocephalus often fail. The surgical procedures chiefly used either aim at the creation of a new communication between the ventricles and the subarachnoid space (2, 3, 6, 7, 8), or at the restoration of the normal fluid passage through the aqueduct (1, 4).

Of the 71 cases of non-neoplastic obstruction of the aqueduct admitted to this clinic, 62 have been operated upon. In 29 cases, the aqueduct was catheterized and a rubber catheter was left in situ for a few days, leading out through the neck muscles. In the remaining cases, a ventriculocisternostomy or some other procedure was carried out. The material is summarized in Table 1, which gives a general idea of the surgical methods used and the operative results. These have been rather disappointing both with regard to operative mortality and late results. It is evident that further experience with different methods is needed to solve the problem of the best surgical treatment in these cases. In this report a description is given of an operative procedure which has been worked out and used in this clinic during the last years.

METHOD

In the surgical treatment of atresia of the aqueduct, the direct approach to the obstruction appears to offer certain advantages. The lesion can be definitely verified and the normal passage of the cerebrospinal fluid restored. As far as our experience with temporary aqueductal drainage goes, catheterization of the aque-

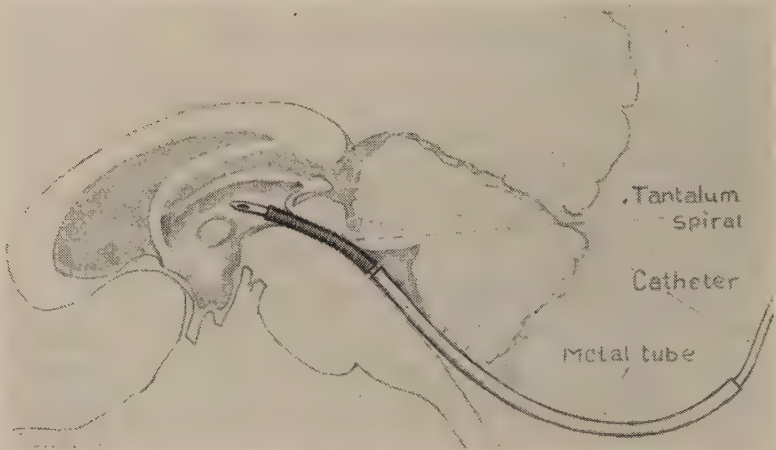


Fig. 1.

After catheterization of the aqueduct, the metal spiral is inserted, threaded on the catheter together with a metal tube, and by means of the tube it is kept in place while the catheter is withdrawn.

duct carries very little risk in itself, and is usually performed without difficulty. The outcome wholly depends on whether or not the passage of fluid remains free. It seems that the only way to obtain this is to perform a reconstruction of the aqueduct by permanently leaving a tube of some kind in the aqueduct after catheterization. In the present method a thin spiral of metal wire is used. A tube of tightly wound fine metal wire is light, flexible and gives a minimum of tissue reaction. The operative procedure is technically simple. The usual suboccipital exposure is done. The bone defect need not be very large. After opening the dura and the arachnoid, the cerebellar tonsils are separated and a narrow spatula introduced through the foramen of Magendie.

The 4th ventricle is inspected, and when a clear view has been obtained of the orifice of the aqueduct, a soft rubber catheter, No. 7 or 8 Charrière, is introduced and gently eased through in the direction of the aqueduct. After controlling by suction that the end of the catheter is in the 3rd ventricle, the catheter is

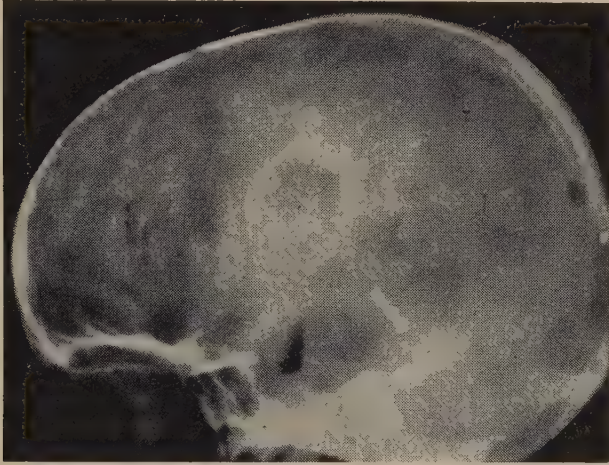


Fig. 2.

Case 1057:44. Postoperative X-ray picture, showing the position of the metal wire spiral in the aqueduct.

withdrawn. The spiral of metal wire is threaded on to the end of the catheter and introduced into the aqueduct. With the aid of a bent silver tube on the catheter, the spiral is adjusted into the correct position and kept in place while the catheter is being withdrawn (Fig. 1). It is of the utmost importance that the spiral, which has a length of approximately 30 millimetres and a diameter of about 3 millimetres, is correctly placed, with about 5 millimetres in the 3rd and 4th ventricles, respectively. The best material for the spiral is tantalum wire, about 0.2 millimetres thick, tightly wound into a tube. After controlling that the spiral is correctly placed and the fluid running freely from the 3rd ventricle, the dura is sutured and the wound closed in the usual

TABLE 1.

Operation	Number of cases	Operative fatality	Well or improved	Un-improved
Catheterization of aqueduct + temporary drainage	29	13	9	7
Ventriculocisternostomy. Dandy	2	2		
Ventriculocisternostomy. Tor-kildsen	4	2	1	1
Ventriculocisternostomy. Hyndman	3	2	1	
Ventriculocisternostomy. Lateral ventricle — cisterna ambiens ..	4	1	1	2
Explorative craniotomy	5	3	1	1
Insertion of tube in aqueduct ..	2		1	1
Aqueductal reconstruction, metal spiral	13	4 ¹	7	2
	62	27	22	11
Ventriculography; no operation	9	4		5

way. In Fig. 2 an X-ray picture (case 1057:44) shows the position of the spiral after operation.

RESULTS

After experimenting with tubes of plastic and silver in a couple of cases, a total of 13 patients have now been operated on with reconstruction of the aqueduct by this method.

Preoperative ventriculograms were made in all cases and showed the typical picture of very pronounced hydrocephalus with occlusion in the proximal part of the aqueduct (5). After operation a dye test or a ventriculogram was usually performed in order to control the passage through the aqueduct.

In 3 cases the operation was performed on infants of 3 weeks and 8 and 9 months, respectively, with extreme congenital hydrocephalus, in order to test the practicableness of the method in similar cases. In one, who also had an Arnold-Chiari malforma-

¹ In 2 cases a ventriculocisternostomy was performed previously.

tion, a ventriculostomy of the 3rd ventricle had been performed previously. Two of the children died in hospital and the other shortly after being discharged. It is doubtful whether operative intervention is on the whole indicated in this group of extreme cases.

The method was used in 10 typical and less advanced cases of atresia of the aqueduct in older children and adults. These 10 cases are summarized in Table 2. Two of the patients died in hospital. One was a girl, previously operated on according to Torkildsen, who died from wound infection and meningitis. The other was a 5-year-old boy with advanced hydrocephalus, who, in addition to the aqueductal obstruction, also had an Arnold-Chiari malformation, platybasia and syringomyelia. A third patient, after a good recovery, died in her home one year after operation. The remaining 7 patients are alive and well, with an observation time ranging from 4 months to 4 years and 6 months after operation. One girl, now 15 years old, who was operated on in 1944, is free from symptoms and doing well at school. Prior to the operation she had epileptic fits, which have subsided. A 9-year-old boy 3 years 10 months after operation still has a somewhat unsteady gait, and attends a class for backward children, but on the whole manages well. A 7-year-old girl is now in good health three years after operation and has been transferred from a special class to the regular school-class. A 21-year-old woman is free from symptoms eighteen months after operation and has had a child. A man of 21 years is now, one year after operation, well and working at full capacity. A 58-year-old business manager still, 7 months after operation, has an occasional headache, but has resumed his work. Finally, a woman of 22 years, operated upon 4 months ago, has made a good recovery and is working at full capacity as a school teacher.

Case	Age Sex	Clinical data	Operation
<i>Ståhl</i> 552:39	10 F	Headache, 4 years; failing vision, listlessness. Secondary optic atrophy.	Aug. 31, 1939. Torkildsen operation. Sept. 9, 1944. Aqueductal reconstruction, gold spiral.
<i>Persson</i> 1057:44	8 F	Headache, 2 years; epilepsy. Choked discs.	Nov. 24, 1944. Aqueductal reconstruction, platinum spiral.
<i>Kjellgren</i> 1157:44	17 F	Headache, vomiting, 6 months; failing vision, diplopia. Choked discs.	Dec. 21, 1944. Aqueductal reconstruction, platinum spiral.
<i>Edwardsson</i> 608:45	9 M	Headache, listlessness, 2 years; unsteady gait, failing vision. Choked discs, ataxia.	July 10, 1945. Aqueductal reconstruction, silver spiral. Aug. 2, 1945. Reoperation. Removal of incorrectly placed spiral and insertion of new.
<i>Wolwan</i> 869:45	7 F	Large head since birth. Epileptic fits, 2 months. No choked discs; strabismus, slight mental retardation.	May 14, 1945. Aqueductal reconstruction, tantalum spiral.
<i>Andersson</i> 154:46	5 M	Large head since birth. Failing vision, 6 months; headache, pain in neck. Choked discs, corneal areflexia left. Platybasia.	April 5, 1946. Aqueductal reconstruction, stainless steel spiral.

Postop. communication test.	Result	Remarks
Dye: no passage	Operative fatality.	After Torkildsen operation catheter removed owing to infection. After aqueductal reconstruction wound infection, death from meningitis 3 weeks postoperatively.
Dye: passage	Living and well. Last report May 23, 1949 (4 years 6 months). Good health. No epileptic fits. Doing well at school.	
Dye, air: passage	Death 1 year 1 month after operation.	Good recovery. Spiral not quite correctly placed and on X-ray 6 months after operation dislodged into 4th ventricle. New dye test showed passage. Sudden death at home. No autopsy.
Air: passage	Living and well. Last report May 4, 1949 (3 years 10 months). Slight unsteadiness of gait, easily tired. Otherwise in good health.	At 1st operation spiral inserted too deeply into 3rd ventricle. After 2nd operation good recovery.
Dye: passage	Living and well. Last report May 6, 1948 (3 years). Symptom free, no epileptic fits. Doing well at school.	
	Operative fatality.	Large infratentorial cyst communicating with lateral ventricle.—At operation spiral incorrectly placed, not reaching 3rd ventricle. Sudden death 3 weeks after op. Autopsy: pronounced platybasia, syringomyelia.

Case	Age Sex	Clinical data	Operation
<i>Johansson</i> 661:46	21 F	Vomiting, headache; 4 years; asthenia, dizziness, tinnitus. Choked discs.	Aug. 23, 1946. Aqueductal reconstruction, platinum spiral.
<i>Magnusson</i> 438:47	21 M	Head injury. Dizziness, 6 months; failing vision, headache. Choked discs.	July 18, 1947. Aqueductal reconstruction. July 30, 1947. Secondary suture of neck muscles.
<i>Nygren</i> 729:48	58 M	After influenza dizziness, headache, 2 $\frac{1}{2}$ years; un- steady gait, hemiparesthe- sia, listlessness. No choked discs. Mental dullness.	Sept. 22, 1948. Aqueductal reconstruction, tantalum spiral.
<i>Pejler</i> 1021:48	22 F	Failing vision, 1 year; headache. Exophthalmus, choked discs, hemiataxia.	Dec. 17, 1948. Aqueductal reconstruction, tantalum spiral. Jan. 13, 1949. Reexplora- tion.

COMMENT

A great many surgical procedures have been proposed and used in the treatment of obstructive hydrocephalus. A number of these procedures have been tried in this clinic, some of them, however, in too few cases to give more than a general impression of the usefulness of the method in question. The method described here has now been in use for some years, and the number of cases is now sufficient to allow a preliminary evaluation of the procedure. So far the results have been somewhat better than with the other methods tried out in this clinic. In some of the cases with fatal issues obvious technical errors have been made;

Postop. communication test.	Result	Remarks
Dye: passage	Living and well. Last report Dec. 10, 1948 (2 years 3 months). Slight impairment of balance. Working at full capacity. Normal confinement July 1947.	
Dye: passage	Living and well. Last report Sept. 14, 1948 (1 year 1 month). No symptoms. Working at full capacity.	
Not performed	Living and well. Last report May 4 1949 (7 months). Occasional headache, work resumed, half capacity.	Pronounced stenosis, but no complete atresia of the aqueduct. Postoperative meningeal irritation. Intrathecal penicillin treatment.
Dye, air: passage	Living and well. Good recovery. Last report May 5, 1949 (4 months). Slight unsteadiness of gait. Working at full capacity.	After 1st operation dye test negative. Reexploration of the aqueduct showed free passage of fluid.

either the tube has been incorrectly placed or it has been too short. With increased experience this can probably be obviated. In the cases where the operation has been technically adequate and a free communication for the cerebrospinal fluid has once been established, the subsequent course has been satisfactory. In these cases a definitive reconstruction of the aqueduct has apparently been achieved. A continuation of the work with this method therefore seems justified. As mentioned previously, the problem of the surgical treatment of atresia of the Sylvian aqueduct can only be solved by further clinical experiences with various operative procedures.

SUMMARY

The experiences of this clinic in the treatment of atresia of the aqueduct of Sylvius is briefly summarized. A new operative procedure for this condition is described, involving a reconstruction of the aqueduct by means of a spiral of fine metal wire. The results obtained with this method are reported.

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On Epilepsy in Sturge-Weber's Disease

By

MOGENS LUND

HISTORICAL NOTE

The coexistence of facial naevus flammeus and glaucoma was first observed by *Schirmer* in 1860. Later, in 1879, *Sturge* reported a similar case with focal epileptic seizures. He assumed that the convulsions were due to a "port-wine mark" on the brain surface. In 1901 *Kalischer* was able to corroborate the presence of the cerebral affection pathologically. In 1922 *Weber* demonstrated the calcifications, characteristic of the disease, in the radiogram. Similar radiographic changes were observed, though never reported, by the Dane *Wissing* in 1921. *Weber* believed that the calcifications were localized in the pial angioma. But *Krabbe* (1934) demonstrated that the cortex underlying the angioma was the seat of these changes. In 1936 *Bergstrand* and *Olivecrona* gave a complete survey of the pathological and clinical aspects of the condition.

PATHOLOGY

Sturge-Weber's disease is by now conceived of as an abnormal development of the primordial vascular pattern. The angioma may affect the face (naevus flammeus), the chorioid, and the pia. The facial angioma may be bilateral, but it is usually unilateral and confined to the area of the first and second branches of the trigeminal nerve. It is rare for the cutaneous angioma to be ex-

tensive and to cover larger areas of the skin. The chorioidal angioma is associated with glaucoma, either congenital or secondary. The pial angioma is usually localized in the occipital lobe. It may involve the parietal and temporal lobe as well, but it is rare for the affection to extend over the entire hemisphere. The teleangiectasies can usually be traced into the cortex. In more severe cases the cerebral tissue, in particular the cortex, is the site of atrophic changes. It is not clear whether these changes are to be considered as developmental abnormalities (*Krabbe* and others) or as secondary to the pial angiomatosis on the basis of nutritional disturbances (*Peters* and others). The characteristic calcifications in the cortex underlying the pial angioma may be found both in the immediate vicinity of the capillaries and in the cerebral tissue without definite evidence of connection with the vessels. The presence of calcifications is usually coincident with a marked atrophy of the neuronal elements. The vermiform double-contoured shadows characteristic of the calcifications are readily demonstrable in the radiogram.

SYMPTOMS

The cerebral symptoms usually make their first appearance in early childhood. The initial symptoms are convulsions and, occasionally, signs of loss of function. Congenital hemiplegia may be seen. Marked intellectual reduction is common. It should probably be considered more as secondary to the fits than as a primary imbecility. Frustrane cases are no uncommon occurrence. Naevus flammeus and glaucoma may be found in cases with no signs of cerebral affection. And the angiomatosis may affect the pia exclusively.

CASE REPORTS

The cases reported below are the first 6 cases verified in the Neurosurgical Department, Rigshospitalet, Copenhagen (E. Busch). All had epilepsy and all have been operated upon.

Case 1. RH. Nkir. 1409. A boy, aged 6. No history of naevi, epilepsy or imbecility in the family. Delivery normal. Otherwise normal until the age of nine months when he suddenly fell ill with a raised temperature, loss of consciousness, convulsions, and strabismus. He recovered during the following 4 days. One month later twitchings of the eyelids occurred, first on the left and later on the right as well. He was admitted to an ophthalmological department where left-sided convergent strabismus was disclosed. Roentgen-examination of the skull showed oxycephaly with premature closure of the sutures. On the basis of this diagnosis a "decompressive" craniotomy was performed, when the boy was a little more than one year old. Since then he has with increasing frequency, and often several times a day, had twitchings of the orbicular muscle and momentary blunting of consciousness. This was at times associated with swaying and fall and additional twitchings of the right arm and conjugated deviation of the eyes upwards. For six months he had had fits initiated as described above, and followed by clonic convulsions in both arms and the left legs, which, in turn, were immediately followed by convulsions limited to the left-sided extremities. The fits were associated with loss of consciousness. Eventually he became deteriorated, manic, and untractable. Occasionally he complained of headache. No effect of phenobarbiturates.

Examination. Naevus flammeus in the right frontal region, the right upper eye-lid, and the right side of the nose. No marked intellectual reduction, mental state as described above. The right optic disc was a little more reddish than the left. The right iris of a somewhat deeper brown than the left. No sign of glaucoma. A radiogram of the skull showed typical calcifications in the right occipital region. Neurological examination revealed nothing abnormal. There was hardly any hemianopia.

Operation. The skull and the dura were abundantly vascularized. A typical Sturge-Weber lesion was found in the right occipital lobe and the contiguous parts of the right parietal and temporal lobes. Occipital lobectomy and sub-cortical extirpation of the temporal lesion were performed.

Microscopy. Thickening of the dura, with proliferation and hyperaemia of the vessels, numerous old and recent haemorrhages. The deep capillary layer is the site of perivascular infiltrations and a notable proliferation of the capillaries communicating with the intradural haemorrhages. The pia is hypertrophied, and the seat of several angiomatous plaques. No calcifications. In the external layers of the cortex just below the glia membrane there is a lining of lime granules most often without connection with the vessels. The cortex is abnormally vascularized. In the white matter there are hypertrophy of glia and some calcifications.

Follow-up. One year after operation he was admitted to an asylum (I.Q. Binet-Simon: 62). No seizures since operation.

Comments. A naevus in the area of the first branch of the trigeminal nerve and calcifications in the occipital lobe were

disclosed. No glaucoma. Intellectual reduction, hardly congenital. No signs of loss of function. The sudden and early onset is characteristic. This is probably the first demonstration of the fact that, as might have been expected, calcifications, may make their first appearance after a period of time, even years.

Case 2. RH. Nkir. 2419. A girl aged 8. Mother's sister was reported to have naevus flammeus in the face and suffer from headaches. No convulsions. In the present case a naevus flammeus was disclosed on the left cheek. Normal development. Always left-handed, though she writes and eats with the right.

8 months before admission she suddenly lost consciousness for 6 hours. When she "came to", she experienced transient disorder of speech of the expressive type. The next day there were numerous twitchings in the right side of the face and a few twitchings in right-sided extremities. No paresis. During the same day she had 3 minor and 5 major fits. Following hospitalization she had no seizures for a period of seven months. Then, in one day, 3 minor fits and 1 major one. Since then occasionally minor fits. For 3 months transient scintillations without lateralization in the visual fields.

Examination. No mental changes. Neurological and ophthalmological examinations normal. Roentgen-examination of the skull revealed no definite calcifications. Ventriculography: slight dilatation of the left lateral ventricle. Pressure not raised.

Operation. The vascularization of the bone was normal, while the dura was bleeding somewhat. A typical teleangiectatic angioma, measuring 1×1 cm, localized in the lower part of the left precentral gyrus was left untouched. A similar affection in the middle of the superior temporal gyrus was coagulated.

Comments. This is one of the extremely rare cases of familial occurrence of naevus flammeus. In this case, too, the onset of epilepsy is acute. The long symptom-free periods of time are characteristic. (The present case has not been histologically verified, but the typical picture at operation together with the naevus flammeus ensures the diagnosis). The localization in the cortex is atypical.

Case 3. RH. Nkir. 1650. Male aged 34. Father alcoholic, died 50-60 years old in status epilepticus. Mother also alcoholic.—Congenital naevus flammeus on the right upper eye-lid. From the age of 5 he had had 6 generalized convulsive seizures. For the last 5 years no seizures, but occasionally slight twitchings in the throat. For an unknown period of time minor fits. In childhood untractable, from early youth an alcoholic. For the last 9 years in a mental

hospital. At intervals psychotic with manic and aggressive traits. During the last years quiet and unaggressive.

Examination. A hypertrophied naevus flammeus on the lateral part of the right upper eye-lid, left-sided hemiachromatopsia. Neurological examination otherwise normal. No glaucoma. On admission he was in a quiet mental state. No oligophrenia. Roentgen-examination of the skull: typical calcifications in the right occipital region, extending into the temporal region.

Operation. A typical Sturge-Weber affection was disclosed in the cortex of the right occipital lobe and the lower, posterior part of the temporal lobe. Occipital lobectomy and extirpation of the affected cortex in the temporal lobe were performed.

Microscopy. The dura normal. No proliferation of pial vessels. Enormous lime deposits in all layers of the cortex, though in some areas between the external and internal granular layers only. In the deeper parts of the cortex there are lime granules in almost every vessel wall, most of which are the site of proliferation of connective tissue. In the deeper parts of the cortex the capillary network is more developed than usual. In some areas the nerve cells are almost completely replaced by calcifications and hypertrophied glia.

Postoperative course. Necrosis of the bone-graft, which eventually had to be removed. No epileptic seizures, but periods of hallucinatory and paranoid states. Marked paresis of the arm and slight weakness of the leg.

Comments. The outstanding features of the present case are alcoholism, probably hereditary in nature, and periods of manic psychosis. Epilepsy was without focal signs and was further characterized by the long symptom-free periods.

Case 4. RH. Nkir. 937 (earlier reported by Krabbe 1934 (G.V.S.)). A female aged 29. Congenital naevus flammeus on the left side of the forehead and on the upper eye-lid. From the age of 3 she had suffered from minor fits up to 4 times daily. On these occasions she stared, turned pale, and sometimes fell. From the twelfth year generalized convulsive seizures approximately once a month, without aura, but associated with loss of consciousness. In periods restless, irritable, and teasing. For the last 16 years committed to "Filadelfia", hospital for epileptics.

Examination. Naevus flammeus on the right upper eye-lid extending over a small part of the frontal region. Right-sided pericorneal and subconjunctival naevus. Intraocular pressure not raised. Left-sided homonymous hemianopia. Apart from these nothing abnormal on neurological examination. Mental state: euphoric, demented. Roentgen-examination: calcifications in the right occipital region, extending into the posterior part of the temporal region.

Operation. Marked thickening of the skull, profuse bleeding from the dura. Teleangiectasies in the pia over the entire occipital lobe and the major part of the temporal lobe, almost reaching the temporal pole. Afferent vessels from

the middle and posterior cerebral arteries. Occipital lobectomy and cortical resection of the temporal affection.

Microscopy. The pia is transferred into an angioma. Large amounts of lime granules in the cortex below the large ganglion cells. No calcifications in pial and cerebral vessels. The external layers of the cortex show normal cyto-architectonic.

Follow-up. During the following 7 years practically no seizures, discharged from "Filadelfia", now able to work in periods.

Comments. In the present case were disclosed a small naevus in the area of the first branch of the trigeminal nerve and a circumscribed cerebral lesion, typically localized in the occipital lobe, with an extension into the posterior part of the temporal lobe. Since early childhood minor fits and non-focal generalized seizures; severely incapacitated; following extirpation her condition improved strikingly.

Case 5. RH. Nkir. 544. A boy aged 13. No familial history of epilepsy, imbecility nor naevi. Delivery normal. From the age of 3 months he had suffered from convulsions. At first there were merely twitchings of the right fifth finger and of the right corner of the mouth. From the age of 8 years generalized seizures associated with loss of consciousness. Since early childhood—perhaps congenital—paresis of the right hand, eventually developing into a severe right-sided hemiplegia with apraxia. He did not talk until he was 6 years old and never learned to talk and write properly. Always fond of music. Apart from his aphasia there was hardly any congenital intellectual reduction, but following the seizure he became mentally blunted. Always forced deviation of the eyes to the left. He had had prodromata during which he would cover his eyes with both hands and act as if he were scared (visual auras?).

Examination. No naevi. Severe right-sided spastic hemiplegia with hypoplasia of the limbs. No definite hemianopia. No excavation of the optic discs. No rise in intraocular pressure. Mental state: expressive aphasia, possibly some degree of intellectual reduction. Obese. Roentgen examination: typical calcifications in the left occipital, parietal, and temporal regions.

An observed fit. Clonic convulsions and turning to the left the head. Conjugated deviation of the eyes to the right. Then turning of the head to the right followed by tonic spasms in right-sided extremities and later also in the face, of about twenty minutes' standing. Then again clonic convulsions in right-sided extremities, immediately followed by left-sided convulsions, lasting about 1 minute. This was, in turn, followed by a short tonic phase and finally by a post-ictal state of sopor during which there was deviation of the eyes to the left.

Operation. Coverings and skull were richly vascularized and bleeding. A large Sturge-Weber affection was extending over the occipital lobe and the

posterior part of the parietal lobe. The affection was covered by a thick layer of jelly-like slightly xanthochromatous fluid. A smaller affection not contiguous with the above in the anterior part of the temporal lobe. Excision of a small area in the occipital and parietal regions. Coagulation of the remaining part of the lesion.

Microscopy. Thickening of the dura. Increase in the number of vessels. Marked angiomatosis of the pia. Typical calcifications in the cortex.

Comments. This case belongs to the small group in which no naevus is found. The cerebral lesion is typical and relatively extensive. The resulting severe epilepsy and signs of focal loss of function were made manifest as early as the third month.

Case 6. RH. Nkir. 1037. A male aged 21. No history of naevus or epilepsy in the family. From the age of three months he had convulsive seizures, occasionally several a day. At first the attacks were both nocturnal and diurnal, but later they occurred preferably just before his falling asleep. Aura: paræsthesias (bilateral?) in toes or fingers followed by twitches in the right side of the face and in right-sided extremities. This was associated with disorder of speech, occasionally with fall, but never with loss of consciousness. A transient post-ictal right-sided hemiplegia was disclosed. Though treated with phenobarbiturates there was a definite increase in attacks. Eventually he developed a persisting right-sided hemiplegia.

Examination. No mental changes. No naevi. Left-handed, probably induced due to the right-sided hemiplegia; the latter was more marked in the lower limb in which some muscular wasting was found. Right-sided astereognosis. Some stuttering, but no aphasia. A slight right lower facial weakness. Ophthalmological examination normal. Roentgen examination showed typical double-contoured calcifications in the left parietal region.

Operation. Profuse bleeding from skin and bone, the latter was thickened. The dura was abundantly vascularized and was slightly adherent to the greyish, thickened arachnoid. The subarachnoidal space above the Sturge-Weber affection was filled up with a jelly-like semifluid layer. The affection was extensive, covering the parietal lobe, except parasagittally, and the pre-central gyrus. During coagulation of the entire affection paræsthesias and clonic seizures occurred in the right foot.

Follow-up. During the following 4 years the frequency of seizures decreased gradually. During the last two years he has merely had a few vague twitches in the right arm. Completely able-bodied.

Comments. In this case also there is no naevus. The macroscopic appearance of the affection is typical, as are the radiographic changes.

EPILEPTIC SYMPTOMS

To the 6 cases reported here, 138 cases¹ gathered from the literature have been added. This series comprises all cases reported up to 1943. They have been accessible either in the original papers or in exhaustive excerpts. In every case a naevus has been demonstrated and in addition at least one of the following signs: glaucoma, epilepsy, signs of focal loss of function, or typical calcifications in the radiogram. Consequently cases have been included in which naevus and glaucoma are found, but no cerebral symptoms, and in which no radiographic examination has been performed. Of the cases without naevi, only those (5) have been included in which either typical radiographic changes or histological verification have been reported.

¹ Schirmer 1860, Sturge 1879, Horrocks 1883, Lawford 1885, Snell 1886, Galezowsky 1898, Kalischer 1901, Cassirer 1902, Bettmann 1904, Cushing (Cases 1, 2 and 3) 1906, Hebold (Cases 1, 2 and 3) 1913, Vollard 1913, Cockayne 1914, Hagen 1915, Elschnig 1918, Paton & Collins 1919, Freese 1920, Nokamura 1922, Komoto 1922, Weber 1922, Sefar 1923, Duschnitz 1923, Salus (Cases 1 and 2) 1923, Monsequand & Bernheim 1924, Zaun 1924, Bär 1925, Marchesani 1925, Kiranoff 1925, Voegelé 1925, Günzberg 1926, McRae 1927, Yamanaka 1927, Brushfield & Wyatt (Cases 1 and 2) 1927, Onken 1928, Kaiser 1928, Worster & Drought (Cases 1 and 2), 1928-29, Rawling 1928-29, Voegelé 1928, Brushfield & Wyatt (Cases 3 and 4) 1928, Brushfield 1928-29, Röttle 1928, Krause 1929, Thomson 1929, Aynsley (Cases 1, 2, 3 and 4) 1929, Andelo 1929, Moore 1929, Röttle 1929, Laignel & Lavastine (quot. by Cavel) 1929, Vincent & Heuyer 1929, Ballantyne 1930, Babonneix (quot. by Cavel) 1930, Frigýér 1930, Uiberall 1930, Cavel 1931, Pi 1931, Schaefer 1931, Yakevlev & Guthrie (Cases 9, 10, 11, 12, 13 and 14) 1931, Brock & Dyke (Cases 1 and 2) 1932, Ellis (Cases 1 and 2) 1932, Kostoulas 1932, Rocke 1932, Steiner 1932, Tyson 1932, Crouzon 1933, O'Brien & Porter 1933, Rogers 1933, Dimitri & Ballado 1934, Krabbe (Cases 1, 2, 4, 5 and 6) 1934, Torre 1934, Vannas 1934, Appelmans 1935, Dunphy (Cases 1 and 2) 1935, Kreyenberg & Hansing 1935, Skydsgaard 1935, Perera 1935, Schiötz 1935, Folk 1935, Granström 1935, Knapp, Biro 1936, Kylin 1936, Olivecrona (Cases 1, 2, 3, 4 and 5) 1936, Riser 1936, Schondel 1936, Mehney 1937, Vogts 1937, DeMorrier & Franceschetti 1937, Rønne 1937, Peters & Tebelis 1937, Rumbaur 1938, Goldhammer 1938, Mullen 1938, Koch 1938, Manolesco 1938, Evans & Evans 1939, Davies 1939, Pincus 1939, Nussey 1939, Ehrlich 1941, Jona (Cases 1 and 2) 1941, Goeters 1941, Lomholt 1941, Engelhardt (Cases 1 and 3) 1942, Jørgensen 1943, Suryaninoff 1943.

Out of a total of 144 cases of Sturge-Weber's disease in the broad sense, as has been defined above, 81 had epilepsy (55 per cent). Naturally this figure cannot be indicative of the frequency of epilepsy in cases with cerebral affections, since the latter condition may not be present in all. In the following an attempt has been made to evaluate the frequency of cerebral lesions and the occurrence of epilepsy in that group.

Of the 63 cases without epilepsy 60 had naevus and glaucoma. Only in 3 cases the glaucoma was absent—they were admitted for migraine (Olivecrona 1935, Case 5) and imbecility (Brushfield-Wyatt's Case 1927 and Brushfield's Case 1928-29).

In 30 of these 63 cases radiographic examination of the skull has been reported. 12 showed typical calcifications. Of these 8 had signs of focal cerebral affection and 2 had none: (Olivecrona Case 5: migraine; Evans and Evans 1939: no cerebral symptoms—but in both cases occipital calcifications were found). In 2 cases there was no information as to signs of loss of function. On the remaining 18, in which radiographic examination did not reveal any calcifications, none had signs of loss of function and 1 was imbecile. *This suggests that it is rare for cerebral lesions to occur without symptoms.* Since only 2 of the remaining group of 33 cases without epilepsy and without radiographic examination of the skull showed signs of loss of function (one of them further was imbecile) I find it reasonable to assume that the majority of these cases had no cerebral affection.

Of 81 cases with epilepsy the diagnosis was not substantiated in the radiogram, at autopsy or at operation in 15 cases, but I believe it plausible to assume that all 15 had cerebral affections. From what has been said it seems as though at least 96 cases—and probably no more—out of a total of 144 had cerebral lesions, viz. all cases with epilepsy, with signs of loss of function and with verified calcifications, either coexisting or monosymptomatic. 81 of these had epilepsy i.e. that *epilepsy occurred in 85 per cent of cerebral Sturge-Weber affections.* It is conceivable that this is a maximum estimate, but, as has been suggested above,

there is hardly any reason to believe that the actual figure is considerably lower.

No account has been taken of the age at observation—in particular the last one—in all these calculations. As has been emphasized above, it is reasonable to assume that calcifications may make their appearance with advancing years. And likewise, in the case of Sturge-Weber affections without epilepsy—for instance in a child with naevus and glaucoma—epilepsy may possibly develop later in life. In an attempt to evaluate the probability of that event the age at onset of epilepsy has been related to the age at observation in the non-epileptic group.

TABLE 1.

Age at onset of epilepsy	0-1	1-10	>10	(>20)	unknown
81 cases with epilepsy	42	17	10	(2)	12 ("child": 11)
Age at last observation	0-1	1-10	>10	(>20)	unknown
63 cases without epilepsy ..	5	5	51	(36)	2

From Table 1 it is clear that *in more than half the cases epilepsy makes its first appearance within the first year of life, and that its appearance after the twentieth year is rare* (cf. Olivecrona Case 1, Brock and Dyke Case 1, 1932; both had—relatively small—typical, occipital lesions and in both no sign of naevus, glaucoma, loss of function, or imbecility was disclosed). From the age distribution *in cases without epilepsy* it becomes clear that *the appearance of epilepsy later in life would seem improbable in the large majority of cases*. This possibly also holds for the 12 cases with calcifications but without epilepsy. Of the latter group 9 were more than 10 years old, 7 of which were more than 20 years.

An evaluation of the significance of the extension of the cerebral affection as related to the occurrence of epilepsy is made difficult by the fact that in a large proportion of cases (29 out of 95) we are unable to advance definite statements as to the exact localization of the cerebral lesion, and that the cases without epilepsy were few (14 out of 95). Moreover, it must be rememb-

ered that we cannot conclude from the extension of the calcifications to that of the pial angioma. The latter is presumably more extensive than the former.

TABLE 2.		Cases with epilepsy		Cases without epilepsy	Total
Localization					
occipital (exclusively or comb.)		46	(84 per cent)	9	55
parietal	" " "	23	(88 " ")	3	26
temporal	" " "	23	(88 " ")	3	26
central region	" " "	11	(85 " ")	2	13
frontal	" " "	14	(88 " ")	2	16
occipital exclusively		18	(72 " ")	7	25
Extension					
one lobe		25	(74 " ")	9	34
two lobes		16	(94 " ")	1	17
three or more lobes		13	(87 " ")	2	15
uncertain		27		2	29

The only point worth noting in Table 2 is the relatively low frequency of epilepsy in cases with calcifications confined to the occipital lobe alone (72 per cent). It is difficult to evaluate the relative frequency of epilepsy in different lobes exclusively affected, since, apart from the occipital lobe, this is the case only in a few instances. In the case of less extensive calcifications—irrespective of their localization—the occurrence of epilepsy is also relatively rare. This is probably bound up with the fact that the less extensive calcifications are usually found in the occipital lobe.

The localization and the extension of calcifications as related to the age at onset of epilepsy is evident from Table 3.

TABLE 3.
Age at onset of epilepsy.

Extension	0-1	1-10	> 10	Unknown	Total
1 lobe	9	7	5	4	25
2 lobes	9	4	2	1	16
3 or more lobes	7	3	0	3	13
uncertain	17	3	3	4	27
total	42	17	10	12	81
occipital exclusively ..	7	4	5	2	18

Although nothing definite can be stated on the sole basis of these figures, they seem to indicate that the less extensive the calcifications the later the appearance of epilepsy. This is possibly due to the above mentioned fact that a relatively large proportion of less extensive lesions are confined to the occipital lobe. Thus in occipital lesions there is not only a lower incidence but also a later appearance of epilepsy.

The relationship between the extension of the cutaneous naevi and the occurrence of epilepsy or cerebral changes as a whole (viz. epilepsy, loss of function, calcifications) is represented in Table 4.

	Cases with epilepsy	Percentage	Cases with cerebral changes as a whole	Percentage	Total
Bilateral naevus	21	(48)	29	(68)	44
Unilateral naevus	53	(57)	59	(63)	93
No naevus	7		7		7
Naevus outside the trigeminal area	17	(49)	23	(66)	35
Naevus within the trigeminal area ..	57	(56)	65	(64)	102

From Table 4 it becomes clear that *the frequency of epilepsy is not higher in patients with bilateral naevi and naevi outside the trigeminal area* than in those with unilateral naevi or naevi within the trigeminal area. If anything, it seems as though the converse holds.

TABLE 5.
Age at onset of epilepsy.

	0-1	1-10	> 10	Unknown	Total
Bilateral naevus	13	1	1	6	21
Unilateral naevus	27	13	7	6	53
No naevus	2	3	2	0	7
Naevus outside the trigeminal area	10	2	2	3	17
Naevus within the trigeminal area	30	12	6	9	57
Total with epilepsy	42	17	10	12	81

From Table 5 it will be apparent that there is no definite inter-relation between the extension of cutaneous naevi and the age at onset of epilepsy, though there seems to be a tendency for

epilepsy to occur earlier in cases with bilateral and extensive naevi. This may be ascribed to a certain degree of parallelism between the extension of the cutaneous and the pial naevi.

Signs of loss of function as related to epilepsy. *Hypoplasia* of the limbs was found in 24 cases, 22 of whom had epilepsy. 22 of the 24 cases had paresis and epilepsy. *Paresis* was found in further 21 cases, out of which 18 had epilepsy. Of the remaining 15 with loss of function, viz. hemianopia, loss of power, and sensory disturbances, epilepsy occurred in 10 cases and was absent in 5. Of the latter 5 cases 4 had hemianopia alone—3 with calcifications in the occipital region, 1 was not examined radiographically, —and 1 only had signs of pyramidal lesions (calcifications in the temporal lobe). In spite of involvement of the parietal lobe in 40 per cent of the verified cases the report of *sensory disturbances* is rare; they are mentioned in 5 cases all of which had epilepsy. *Hemianopia* was found in 17 cases, out of which 13 had epilepsy. Of signs of loss of function 8 had *hemianopia only*, and the 4 without epilepsy all belonged to that group. This is in accordance with the fact that the occurrence of epilepsy and of visual aura is rare in cases with calcifications affecting the occipital lobe only. And, moreover, it is in harmony with the experience in other intracranial tumours that the occipital cortex is epileptogenic to a less extent than are other cerebral areas.

Thus, out of a total of 60 cases with focal signs 50 had epilepsy (83 per cent) and in 10 it was absent. The fact that epilepsy did not occur in the last 10 cases cannot possibly be due to the patients' being particularly young since in the 8 cases in which the age at verification or at the last examination is known, they were older than 10 years.

The time of onset of epilepsy as related to that of signs of loss of function. Out of 40 cases with both paresis and epilepsy, paresis was present before the onset of epilepsy in 9, all of which had convulsions within the first year of life, except for 2 cases in which information could not be obtained. Further, congenital hemiplegia was present almost in all, and in 7 hemihypoplasia

was found. In 14 cases paresis developed after the onset of epilepsy. And as regards this point information was unavailable in 17 cases. *A sudden onset in early childhood* with a state more or less similar to that of status epilepticus is mentioned in 16 cases (for instance the present Cases 1 and 2). This condition is often followed by signs of severe loss of function and a marked rise in temperature. In 7 of these cases there was a symptom-free interval of several years standing before the reappearance of epilepsy. The early symptoms are presumably due to thrombosis or rupturing with ensuing subarachnoidal hæmorrhage of the pial angioma.

Type of Attack. Of 81 cases with epilepsy 17 had generalized, non-focal seizures only, 8 of which had additional minor fits. 11 had both focal and non-focal fits and 2 of these further minor fits. In 39 cases the fits were focal, 3 had additional minor fits. 2 had minor fits alone. The type of the attack was not reported in 12 cases. Minor fits (absence, petit mal) have been reported only in 15 cases, but the fact that 4 of the present 6 cases had minor fits seems to indicate a more common occurrence. Despite the common involvement of the temporal lobe (40 per cent of the verified cases) dreamy states have not been reported.

Auras. In a large proportion of cases (34) no mention has been made of the presence or absence of auras. In 15 cases no aura occurred while 19 cases had motor auras; 4 sensory, 4 vague visual hallucinations, 1 more elaborate ones, 1 aphasia, 1 hallucinations of smell and 2 uncharacteristic auras. The rare occurrence of visual, so-called temporal and sensory auras is striking considering the favoured localization of the lesion to the posterior parts of the hemisphere. On the other hand, it must be remembered that in many cases the reports are insufficient and that the majority of cases are children.

The Localization of the Initial Symptoms. Focal fits often appear as conjugated deviation of the eyes and turning of the head only—or these phenomena may herald other signs (15 cases). This may be considered a result of irritation of the occipital eye

field. In other cases the initial irritation seems to be localized in the face area (5 cases), the arm area (5 cases) or in both (6 cases); in 3 cases the arm and leg areas were simultaneously involved and in only 1 case the leg area was the site of the initial irritation. In 15 cases no information was available.

The Initial Epileptic Paroxysm was a focal fit in 40 cases; a non-focal one in 21 cases and a minor fit in 5. Since the patients are usually infants the information of course is not too reliable. In 15 cases no information was available.

Symptom-free intervals often lasting several years have by most authors been considered one of the characteristic features. It has been reported in 21 cases (cf. the present cases 2 and 3).

Headache of a migraine character has been described in 7 cases; occasionally occurring as an equivalent of a fit.

Hereditary disposition to epilepsy is mentioned in 8 cases, all with epilepsy (cf. the present case 3). A familial occurrence of naevus flammeus seems to be rare and has been reported in only 1 case (the present Case 2). *Granstroem's* case has not been included since naevus was the only sign. *Pentfield* and *Geyelin's* much quoted case of "Cerebral Calcification Epilepsy" is hardly to be classified as a Sturge-Weber disease.

Special mention should be made of the 7 cases without cutaneous naevi. None of them had glaucoma so that the diagnosis depended upon the presence of calcification, which was actually demonstrable in all, and all had epilepsy—(viz. *Brock* and *Dyke* Case 1 1932; *Krabbe* Case 2 1934; *Kylin* and *Kjelin* 1936; *Olivecrona* Case 1 and 2 1936; present Cases 5 and 6). On the whole the onset of epilepsy was late in these cases; 2 were more than twenty years old, 3 were between 3 and 6 years old, and 2 were within the first year of life. The lesion was usually limited to one lobe (5 cases). Loss of function was rare, it was not disclosed in 4 cases. Non-focal attacks occurred only in 1 case (*Kylin* and *Kjelin*)—and in that case no focal signs or symptoms developed later on. This is the only case in which the differential diagnosis between the condition under consideration and "cryptogenic"

epilepsy may be difficult. However, the seventeen year old patient had typical calcifications. Routine radiograms of the skull in all children suffering from epilepsy would undoubtedly disclose more of these cases without cutaneous naevi.

15 cases were operated upon (*Olivecrona's* and the present six cases). As judged from the epileptic symptoms the results were favourable in 10 cases. The remainder could not be evaluated. In suitable cases extirpation seems to give the most favourable results.

DISCUSSION

The striking frequency of epilepsy in Sturge-Weber's disease is not surpassed by that in intracranial tumours (unpublished data). And I doubt that such a frequency is to be found in any other morbid condition in human pathology. There is nothing indicating that it is due to hereditary or otherwise endogenous factors. Nor can it be ascribed to other cerebral malformations—as for instance is the case in cysts of the septum pellucidum. The marked "epileptogenicity" of the condition must be due to the particular pathological changes, i.e. the epilepsy is purely exogenous. Obviously it cannot be due to the involvement of the posterior parts of the hemisphere since cerebral affections are usually the more epileptogenous the nearer the central region. And since intracranial tumours constituting a histological entity are the more epileptogenous the nearer the cortex (unpublished data) one main cause for the high frequency of epilepsy in Sturge-Weber lesions must be their prevailing *cortical* localization.

The presence of the pial angioma leads to circulatory changes in the cortex, in turn resulting in cellular hypoxia and in that state of instability of the nerve cells required for "an epileptic discharge".

SUMMARY

The author gives a *brief survey* of Sturge-Weber's disease, and *reports, in detail*, 6 cases with epilepsy, all operated upon. *From the literature* on this disease 138 cases have been

reviewed, all (except 5) with naevus and at least one of the following signs and symptoms: epilepsy, focal signs, typical calcifications, or glaucoma. In 5 cases *no naevus* was disclosed but they had all typical calcifications.

Out of 144 cases 81 had epilepsy (55 per cent). The majority of cases without epilepsy had both naevus and glaucoma. A survey of the radiographed cases seems to indicate that *cerebral changes without symptoms are extremely rare*. In 96 cases showing signs of cerebral affections *epilepsy was found in 85 per cent*. And it may be assumed that the actual frequency of epilepsy in Sturge-Weber's disease is hardly much less.

In more than half the cases with epilepsy this symptom makes its first appearance within the first year of life. In the remainder *the onset* is more common in childhood than in adolescence; and it is extremely rare for epilepsy to make its first appearance after the twentieth year.

In less extensive cerebral lesions the frequency of epilepsy is somewhat lower than in widespread ones, and the onset is later. This is probably due to the fact that in these cases the lesion is confined to the occipital lobe, which is epileptogenous to a less extent than other lobes.

The occurrence of *epilepsy is not particularly frequent in cases with bilateral naevi or naevi outside the trigeminal area*, but the onset is perhaps a little earlier than in other cases. This is probably due to a certain parallelism between the extension of the cutaneous and the pial naevi.

83 per cent (50 out of 60) of the cases with *focal signs* had epilepsy. In cases with hypoplasia or paresis epilepsy almost invariably developed. A *sudden onset in early childhood* with convulsive seizures, hemiplegia and a rise in temperature is not rare (2 of the present cases). *Focal attacks* are more common than non-focal, generalized, or minor fits. Dreamy-state has not been reported. The auras are usually motor in nature; other types—even visual ones—are rare. *Initial turning of the head and the eyes* is particularly common (irritation of the occipital eye field?).

It is rare for the initial irritative phenomena to occur in the leg. The occurrence of *symptom-free intervals*—often lasting several years—is striking.

Seven cases had *no cutaneous naevus*. In these cases the onset of epilepsy was late, the cerebral affection was not extensive and focal signs were missing or only less pronounced.

The importance of *roentgen-examination* of the skull is emphasized in all cases of epilepsy in children. In selected cases the *results of surgical treatment* are favourable as regards the epileptic symptoms.

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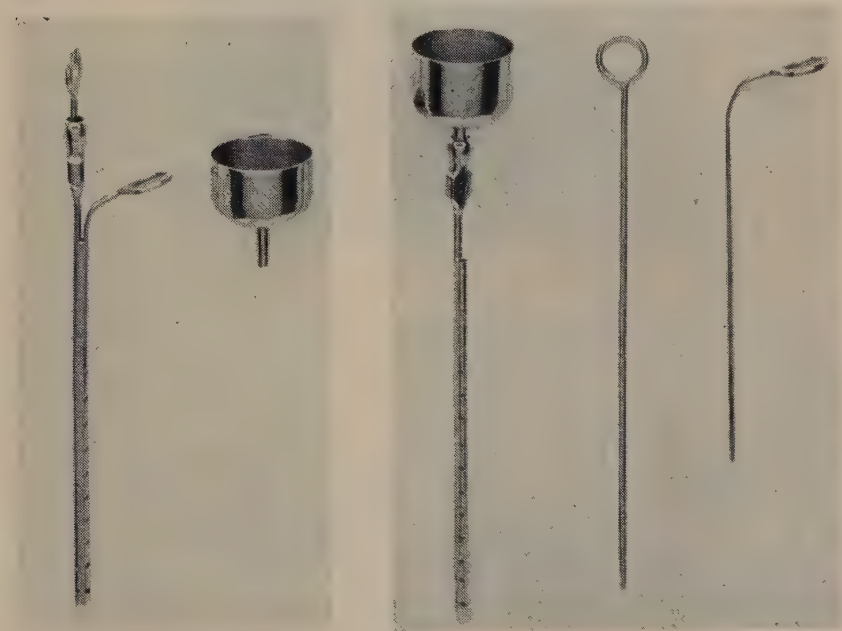
M. Lund, Neurologisk Afdeling, Odense Amts- og Bys Sygehus, Odense.

A Simple Method of Producing a Special Picture of the Posterior Part of the Third Ventricle

By

RICHARD MALMROS

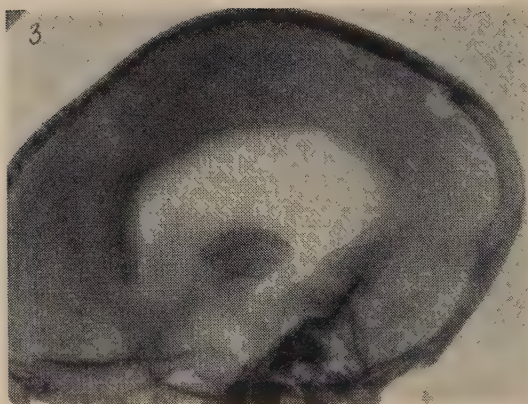
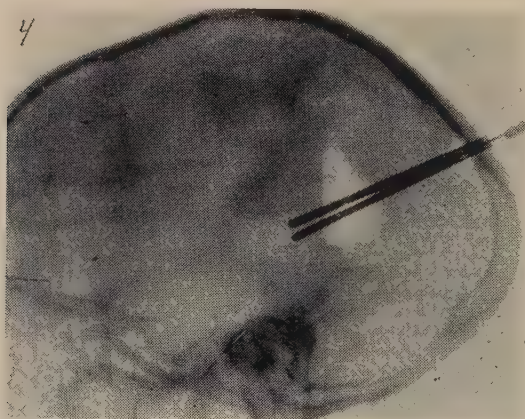
By the method in which ventriculography is usually performed in Scandinavia (photographed according to Lysholm¹) it is fre-



Figs. 1-2.

Special double trocars for refilling the lateral ventricles with fluid (see text).

¹ Erik Lysholm: *Das Ventrikulogram*. Stockholm 1935.

*Fig. 3.**Fig. 4.*

quently difficult to get a clear image of the posterior part of the third ventricle and the aqueduct. Particularly in cases with pronounced dilatations of the lateral ventricles, we may very often see the dense shadows of the air in the lateral ventricles covering the posterior part of the third ventricle and the beginning of the aqueduct, in such a way that it is difficult or even impossible to get a clear view of these structures. Especially in cases where the patients have symptoms due to increased intracranial pressure only and ventriculography shows considerable dilatation of the lateral ventricles and the third ventricle with no air in the fourth ventricle, it is absolutely necessary to get a

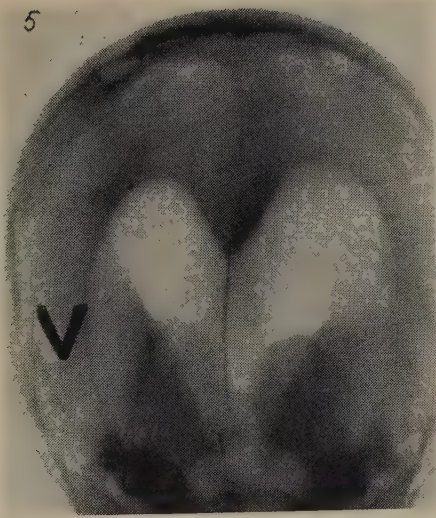


Fig. 5.



Fig. 6.

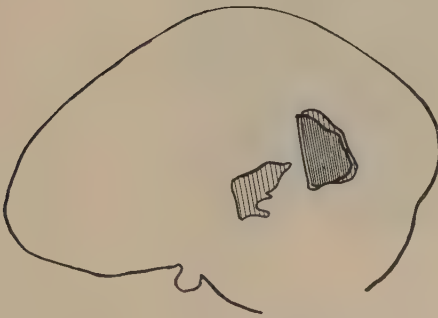


Fig. 4 a.

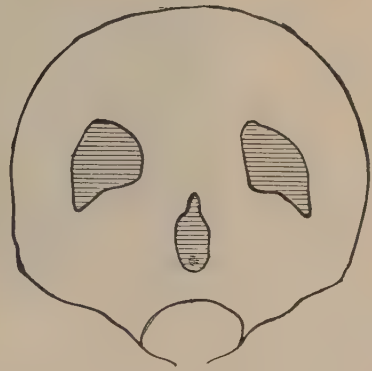
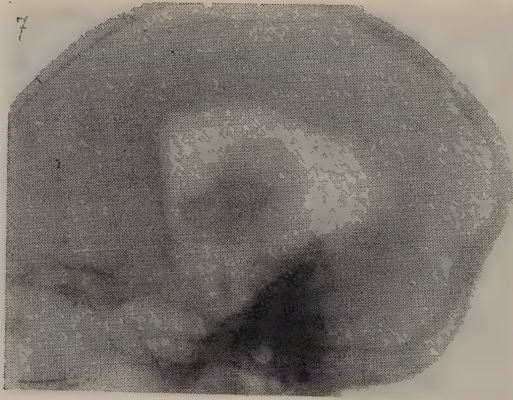
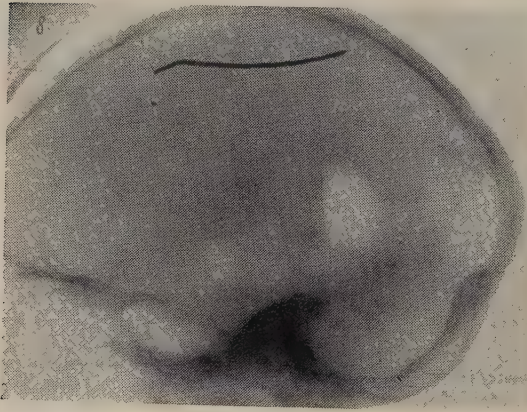


Fig. 6 a.

Figs. 3-6.

Case 1850/45, woman, 28 years, glioma pontis. Figs. 3-5 abundant air in lateral ventricles covering the 3' ventricle.—Figs. 4-6 brain trocars inserted, air removed from the lateral ventricles but remaining in the 3' ventricle and the aqueduct, no air in the 4' ventricle.

clear picture of the posterior part of the third ventricle and the first part of the aqueduct in order to get a correct diagnosis of a pinealoma, of a stenosis of the aqueduct, a glioma of the third ventricle or in the brain-stem.

*Fig. 7.**Fig. 8.*

In such cases we have had great help from a simple method of producing a special picture of this part of the ventricular system.

When ventriculography in the ordinary way has shown itself to be insufficient, the patient is placed prone with his forehead on the x-ray table. Brain trocars are inserted through the burr holes into both of the lateral ventricles. A small funnel is placed in each trocar. On saline solution being poured through the trocar on the left side, a part of the fluid will go through the foramen of Monro (which is never blocked in these cases) into the right ventricle pressing air from this out through the other

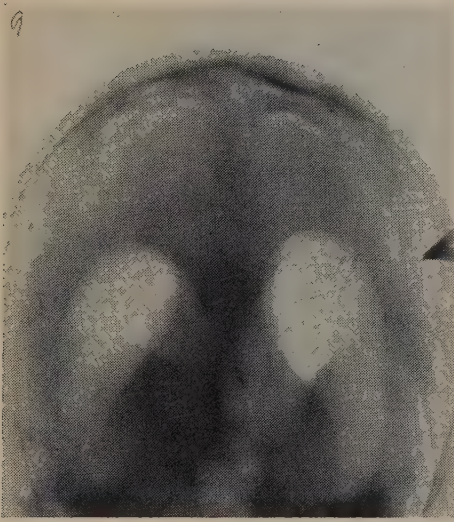


Fig. 9.



Fig. 10.



Fig. 8 a.

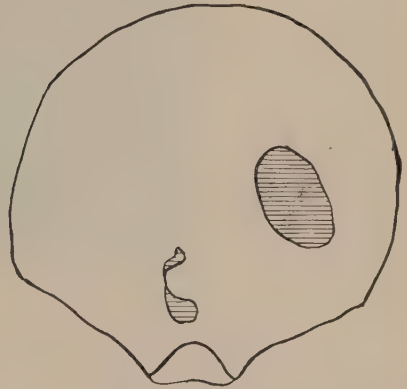
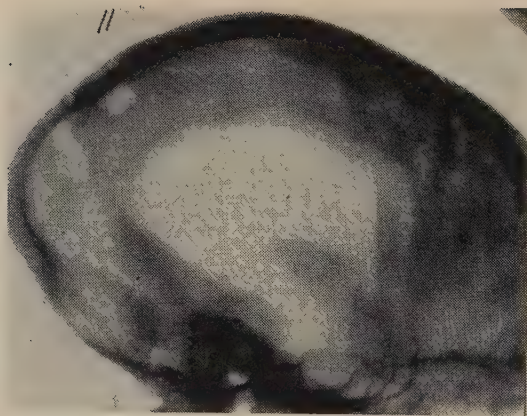
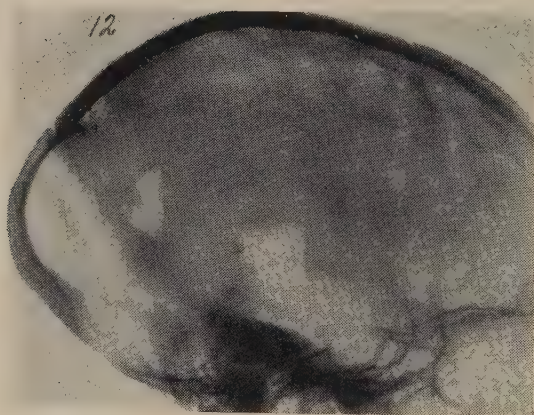


Fig. 10 a.

Figs. 7-10.

Case 2143/46, man, 19 years, glioma profundum hemisphærii sin. Fig. 8 lateral view. A dense shadow is seen in the anterior part of the 3' ventricle, a less dense in the posterior part and a further dense shadow immediately before the pineal body. Fig. 10 post-ant-oblique view, tumour is seen growing into the posterior part of the 3' ventricle from the left side.

trocár. When saline solution then is poured through the right trocar, some air will escape from the left ventricle. By alternately

*Fig. 11.**Fig. 12.**Fig. 12 a.**Figs. 11-12.*

Case 2620/46, woman, 21 years. Stenosis aqueductus.

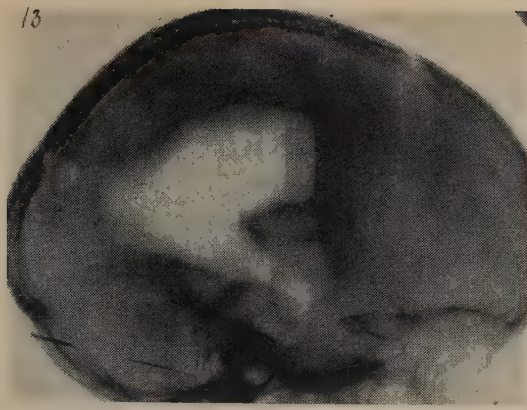


Fig. 13.

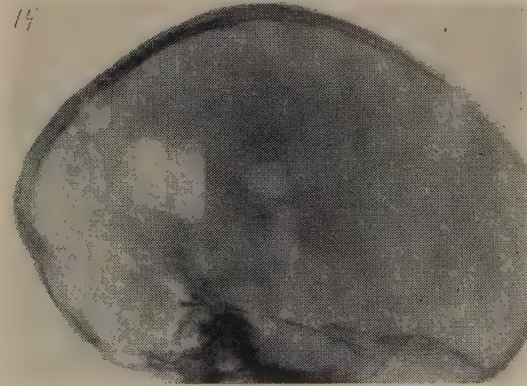


Fig. 14.

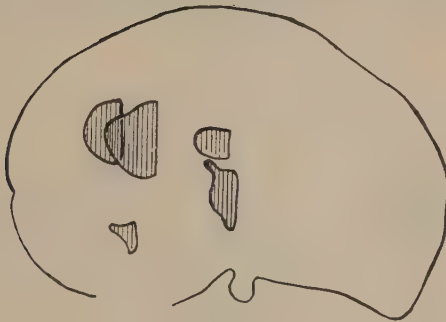


Fig. 14 a.

Figs. 13-14.

Case 1456/45, girl, 8 years, glioma pontis. Fig. 14 air in the posterior part of the 3' ventricle, no filling of the aqueduct, air in the dislocated 4' ventricle. Furthermore air in the posterior part of the ventricle in septum pellucidum.

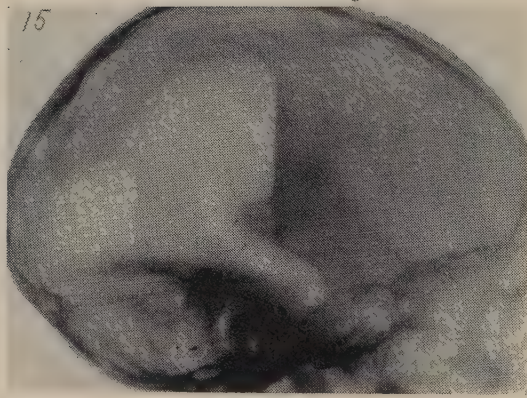


Fig. 15.

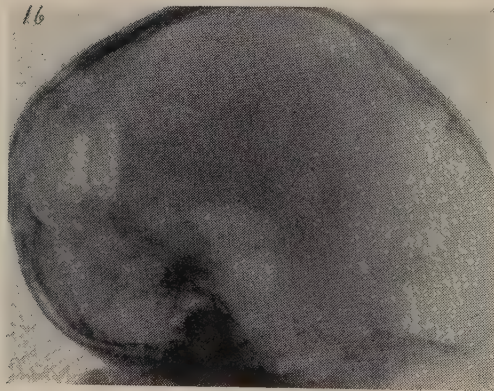


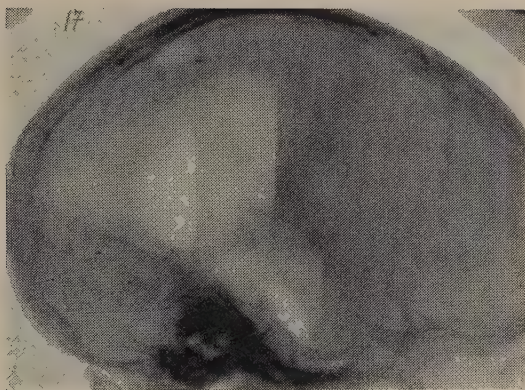
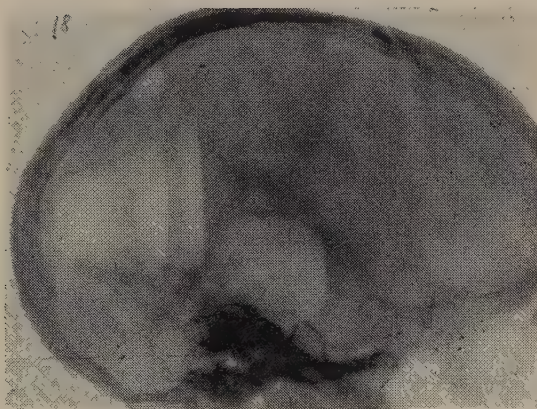
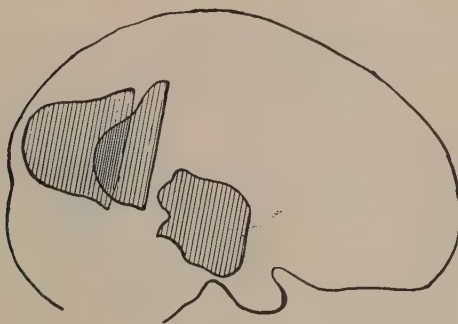
Fig. 16.



Fig. 16 a.

Figs. 15-16.

Case 3090/46, girl, 11 years. Stenosis aqueductus.

*Fig. 17.**Fig. 18.**Fig. 18 a.**Figs. 17-18.*

4873/48, boy, 13 years. Stenosis aqueductus.

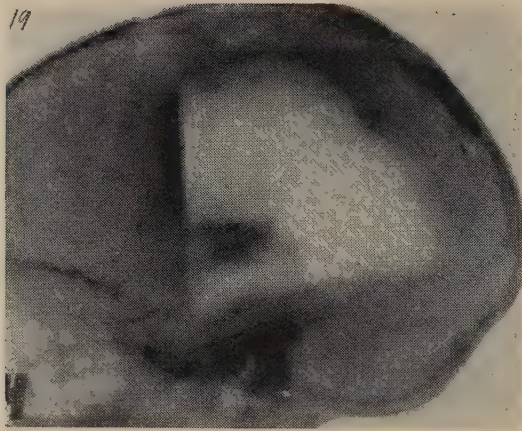


Fig. 19.

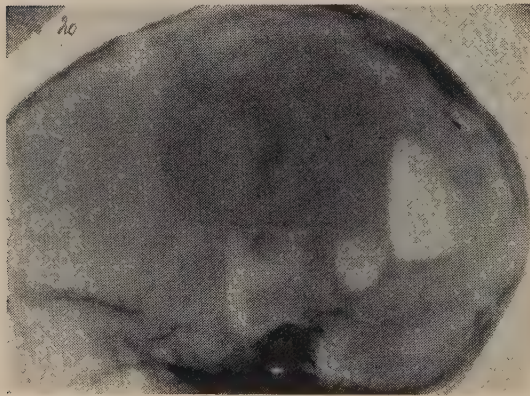


Fig. 20.

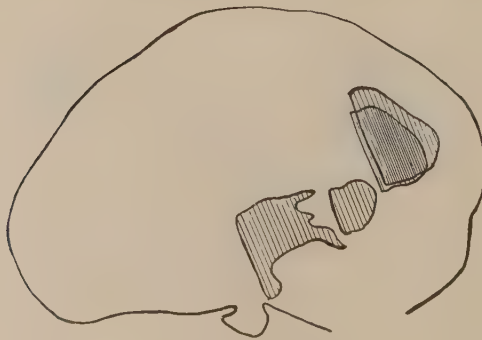


Fig. 20 a.

Figs. 19-21.

Case 1785/45, girl, 8 years, glioma laminae quadrigeminae. Fig. 20 filling of the posterior part of the 3^d ventricle and the dilated aqueduct obstructed by tumour. Furthermore an air pocket in the cisterna v. magna Galeni due to spontaneous perforation of the right lateral ventricle. Compare post mortem picture of the brain with a forceps inserted from the dilated cistern into the lateral ventricle.

*Fig. 21.*

pouring saline solution through the left and right trocar, it is possible to drive most of the air out of both lateral ventricles.

As the head of the patient during this process is fixed with the forehead on the x-ray table, the air will remain in the third ventricle behind the foramen of Monro, and, without altering the position of the head, pictures can now be taken in lateral view and in posterior-anterior oblique view presenting a special picture of the posterior part of the third ventricle and the aqueduct (see figs. 4 and 6).

To begin with we used the ordinary brain trocars for ventriculography but later on we obtained special double trocars as shown in fig. 1. When the trocar is inserted the two mandrels are removed and a small funnel is placed in the longer part through which saline solution is poured causing the air to escape through the shorter (fig. 2).

The following pictures illustrate some of our cases. We have used the method since 1944 in thirty odd cases, and in the majority of these we got valuable information as to the diagnosis. In no cases did the method cause complications.

A Case of Disseminated Sclerosis and Glioma of the Brain in the Same Patient

By

C. J. MUNCH-PETERSEN

Dr. Oscar Bloch, professor of surgery in the University of Copenhagen from 1897 to 1913, in one of his lessons claimed: patients may have more than one disease, but doctors do not know. This sarcastic paradox emphasizes a truth as paradoxes often do. It is true that in attempting to diagnose a malady we will always try to look at the different symptoms from a single point of view as a general exponent of the ailment in question.

Personally I do not remember to have experienced the coincidence of disseminated sclerosis and tumor of the brain.

Nor have I found publications dealing with this subject.

However, I have only explored the question by studying a series of greater neurological text books. Anyway, such a case must be regarded as a curiosity; if only as a curiosity, is a question which will be discussed below.

In what follows a case of disseminated sclerosis will be described. 3 years after the disease was diagnosed, the patient suddenly got unconscious. She was admitted to hospital and succumbed a few hours later.

Case (No. 3064): A woman, aged 49, had a history of "influenza" in April 1939. A fortnight later temporary tingling paresthesia and slight subjective feeling of diminished force of the right arm and leg. Six months later she turned giddy for some months. May 45 the left arm was suddenly paralysed.

This symptom disappeared after 2-3 months. During the summer paresis of both legs gradually developed, accompanied by reeling gait.

February 45 admitted to the Neurological Clinic of the University of Århus.

Examination: Cranial nerves and upper extremities revealed no abnormality except for a slight oculogyric instability.

Nor did the ophthalmological examination reveal any other abnormality. Abdominal reflexes absent.



Fig. I.

Macroscopic section of the tumor.

Lower extremities showed slight ataxia and spasticity without sensory changes.

Babinski's sign could be elicited on both legs.

Gait: Spastic-atactic.

Laboratory data: Blood: normal.

Gastric fluid after histamine injection: normal.

Wassermann reaction: negative.

Cerebrospinal fluid: 14 lymphocytes per cmm.

Total protein per 100 cmm.: 60 mg.

Colloidal-mastix test: "paretic-like curve" with complete "dip" to the left in the first tube.

The patient was treated with neosalvarsan, blood transfusion, and exercises of gait and coordination.

She left the clinic in fairly good condition. The gait was better than before the treatment.

In the following years she was able to perform her domestic duties without difficulty. 8 days before her admission to hospital (Amtssygehuset, Århus) August 12th, 1948, she felt fatigue, but had no other complaints. In the afternoon of that day she suddenly became unconscious and was admitted to hospital.

Examination revealed Cheyne-Stoke's respiration. Slight spontaneous movements of the limbs. Babinski's sign was elicited on both legs.

Ophthalmoscopy: incipient papilledema.

She was unconscious until death occurred at 9 o'clock p.m.

Autopsy (Dr. Tage Lund¹) (Spinal cord not removed): All organs except the brain were normal.

Brain: the left hemisphere enlarged, on frontal sections an orange-sized tumor is seen. The tumor is situated in the external capsule growing downwards and backwards into the mesencephalic part of the brain and into pons



Fig. II.

Tumor as seen at autopsy showing pseudorosette formation.

v. Gieson-stain.

varolii. In the tumor big recent hemorrhages (Fig. I). On closer study of the brain numerous minor disseminated patches were discovered. Some of them symmetrically situated close to the walls of the ventricles. In the upper part of the spinal cord corresponding to the posterior columns a single patch is also seen.

Microscopical study of the tumor: A sharp limit is seen between the tumor and the surrounding tissue. The tumor is formed by cells with little cytoplasm. They show formation of syncytically connected fibrils. Several areas are seen containing a dense formation of fibrils which are surrounded by a wall of centrally radiating tumor cells. Around some of the vessels the same structure is observed with hair-like fibrils close to the walls of the vessels (pseudorosette formation). The nuclei vary a little in size. Some of them fairly big and pale,

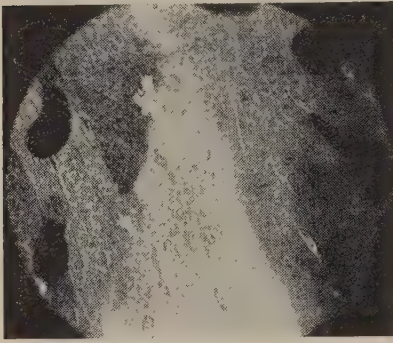
¹ Dr. Lund was kind enough to hand over the brain to me because the patient had previously been treated in my department.

all of them of an elongated shape. In some places the arrangement of the cells is like that found in neurinomas.

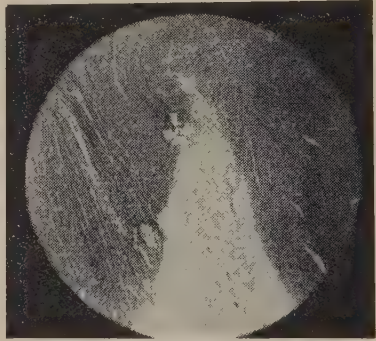
No mitoses are found, neither proliferation of connective tissue nor thrombosed vessels.

Several cells contain blepharoplasts¹ (Fig. II).

Most likely this tumor must be diagnosed as belonging to the group of ependymomas, even if the histological picture is not quite the same as that commonly met with in tumors of this kind.



a: Myelin sheaths stain.



b: Davenport stain.

Fig. III.

Patch from the upper part of the spinal cord.

Surely we do not find the polygonal cells forming the typical circular linings around the vascular channels, but we find the formation of pseudorosettes and blepharoplasts.

At any rate we are dealing with a highly differentiated tumor which without doubt grows very slowly.

Microscopic study of the patches:

Sections stained for myelin sheaths are more or less unstained, and more or less sharply limited patches are seen² (Fig. III a).

Fat stains show very little or no fatty changes and only periferally situated in the patches.

¹ I am indebted to Dr. Erna Christensen for assistance in the histological diagnosis of the tumor.

² I have seen a similar state in some other cases of disseminated sclerosis. These cases will be published later.

Sections stained according to the method of Davenport for axis-cylinders show the patches sharply limited, and the axis-cylinders have almost disappeared in the patches (Fig. III b).

Stains for astrocytes and fibrillary glia reveal very little proliferation of neuroglia, and the amount of astrocytes is small.

The astrocytes present themselves in a marked regressive state. They convey the impression that they are "weak and unable for reaction".

Summarizing the clinical picture and the neurohistological examination of the brain and upper part of the spinal cord (which was removed together with the brain), we have to consider:

(1) Clinically a case which without doubt must be diagnosed as disseminated sclerosis.

(2) Histological changes which must be interpreted as disseminated patches belonging to the histological entity encountered as disseminated sclerosis. On the other hand these changes are not typical. First, in sections stained for myelin sheaths the patches are not sharply defined. Secondly, sections stained for axis-cylinders show a sharp limit of the patches, and the axis-cylinders have almost disappeared in the patches. Thirdly, the fibrillary gliosis is only slightly marked, and the astrocytes are "weak and lazy".

(3) The case is connected with a process of development of glioma belonging to the type of ependymoma.

The death of the patient occurred by a sudden hemorrhage in the tumor. These three points bring about some questions:

It is impossible to decide which of the two changes in the brain is the primary one. Both of them have a fairly slow growth. On admission to hospital in 1945 the symptoms of the patient must be attributed to the disseminated sclerosis only. The transient symptoms are typical for this disease. Furthermore, the symptoms appeared at intervals and were not unilateral.

Examination of the tumor showed only recent hemorrhages.

Finally, the examination of the cerebrospinal fluid, especially

the colloidal-mastix test, indicates that the changes found depend on the presence of a disseminated sclerosis. The increase of the protein of the c.s.f. was relatively small, but the "dip" in the first tube was complete.

A colloidal reaction of this type is only met with in cases of brain tumor where the increase of protein in the c.s.f. is much more pronounced.

However, the histological features of the patches are atypical.

The development of glia fibrils was only poor. The astrocytes were "weak", of outstanding regressive type, and the damage of the axis-cylinders was much more pronounced than that of the myelin-sheaths.

The typically sharply defined boundary of the patches actually was only demonstrable in stains for axis-cylinders and not in stains for myelin sheaths. These phenomena may be due to an individually conditioned lack of reaction of the tissue or to special qualities of the noxious agent. Recent experimental investigations make it probable that this disease is not a circumscribed entity, but a general response of the central nervous system to different noxious agents.

On the other hand, Einarson and Neel suggest that different factors may be responsible for the different reaction of the nervous tissue under pathological conditions, especially belonging to the diffuse sclerosis.

In their published cases of diffuse sclerosis these authors claim to have established transitional cases between diffuse sclerosis and diffuse glioma.

In their paper on the three types of glioblastoma, Busch and Erna Christensen discuss a problem concerned with the pathogenesis of the gliomas. They suggest that the theory of degeneration and that of the rôle played by dysontogenetic factors may be combined with the hypothesis of Einarson and Neel.

These authors put forward four tissue factors:

(1) Insufficiency of the interfascicular oligodendroglia (nutrition of the myelin sheaths).

(2) Insufficiency in the metabolic functions of the microglia.

(3) Actions of atypical metabolic degeneration products on the astrocytic function.

(4) Inherent tendency of macroglia to tumor-building.

Concerning the case mentioned we have found that the myelin sheaths in the patches were severely damaged but had not disappeared. Furthermore, the astrocytes were "weak", apparently badly developed with very little ability to fibrillary response.

In accordance with the hypothesis of Einarson and Neel we have to entertain the possibility that atypical degeneration products inhibit the functions of the astrocytes.

If so it may be that astrocytes thus affected will "change function", a change resulting in tumor formation. However, these theoretical possibilities seem rather arbitrary, especially as we have to presume an inherent tendency of the astrocytes to proliferation. The type of cells found in the glioma is quite different from the astrocytes in the patches, and no patches are found in the neighbourhood of the tumor. Moreover, the evolutionary basis of the two types of cells are different. Transformation of astrocytes to cells of the ependymomic type is thus improbable.

Finally, there are neither any changes of the axis-cylinders and the myelin sheaths in the surroundings of the tumor, nor in the tumor itself, which resemble the changes in the patches.

Most likely the interpretation of the clinical and the histological findings in this case will be an accidental development of disseminated sclerosis and glioma of the brain in one and the same person. Considering the atypical neuropathological features of the patches in view of the hypothesis of Einarson and Neel, we may perhaps assume that diffuse sclerosis and disseminated sclerosis are two different morbid entities.

Apart from the reflections which the case gives rise to its only value is that of a curiosity.

The Function of the Parietal Eye

By

S. H. MYGIND

Quid Saulus inter prophetas?
(1. Samuel. 10.11).

In order to understand certain diseases of the labyrinth, the author has been obliged to build up his own theory of the function of this organ. In trying to do so, a comparison between the motor reactions arising from the skin, the lateral organ, the labyrinth and the eye has proved useful. All these motor reflexes, which serve to maintain the normal position of eyes, head and body, seem to be based on the same simple principles. These are so primitive that corresponding mechanisms may be demonstrated also in invertebrates. We now have tried to apply these principles to the problems of the parietal eye.

The parietal eye is generally regarded as an organ of sight, just as the lateral eyes are, but in a state of more or less advanced degeneration. We will, however, try to show that the parietal eye has never been a picture-producing organ of sight, competing with the lateral eyes. It has a function of its own.

A well-developed parietal eye, with a pigment-free transparent covering ("cornea" or "pellucida" of Studnička), with a parietal foramen, with a lens, corpus vitreum, retina and, at least in the foetal stage, a not degenerated nerve is, in modern animals, found only in the lamprey (*Petromyzon*) and in certain reptiles: the very primitive *Sphenodon*, the so-called "living fossil", and in several saurians.

The organ is apparently unpaired. But it seems sufficiently



na₂ pin my p.brw

Fig. 1.

Head of *Ostracoderm* (Stensjö). pin.: parietal eye. orb.: orbit.
na.: nasal openings.

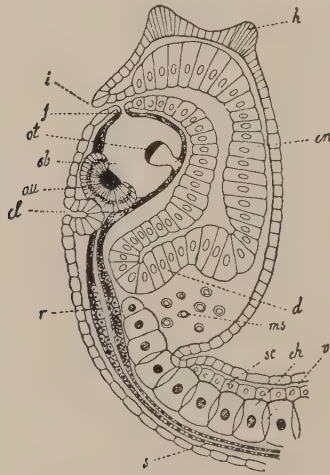


Fig. 2.

Tunicate larva (Jaekel). au.: median eye. ch.: chorda. ot.: otocyst.

established that there is a paired structure. One part of this structure becomes the parietal eye. In the lamprey the other part is pushed forward and becomes the so-called paraparietal organ with a structure fundamentally similar to the parietal eye, which covers it (Figs. 7, 8, 9). In reptiles it is pushed backwards and becomes the epiphysis and pineal gland.

In the earliest vertebrates known, the ostracoderms, which lived about 450 million years ago, we find lateral as well as parietal eyes (Fig. 1). The parietal foramen is situated on the top of the head (as in all other vertebrates mentioned below). It is quite small, while the lateral eyes are large. The parietal eye, therefore, can never have commanded any part of the surroundings outside the visual field of the lateral eyes and we can hardly imagine that it has been of any use as a supplement to ordinary sight.

At a presumably earlier stage in the evolution, an unpaired eye is found in the larva of the tunicates. These probably represent a side branch of forerunners of the true vertebrates. This eye is situated inside an ectodermal cavity belonging to the anterior part of the nervous system (Fig. 2). Another unpaired organ inside the same cavity has been regarded as an organ of equilibrium.

What, then, is the function of the parietal eye?

When the lateral eyes are stimulated by a light ray of suitable intensity and in such a direction that it strikes the fovea, the eye will not move. But if the ray strikes outside this spot, a corrective movement of the eyes takes place and brings them into such a position that the ray now falls within the fovea. Thus, each eye performs a rotating movement directed against the stimulus (Fig. 3). If the light comes from the opposite side, the opposite part of the retina is stimulated and the opposite movement takes place. The two halves of the retina are, so to speak, oppositely orientated.

By following these two rules—the opposite orientation of two oppositely situated parts of a neuro-epithelium and the reactional

movements directed against the stimulus—it proved possible to arrive at a theory that apparently is able to explain all the phenomena of the static part of the labyrinth.

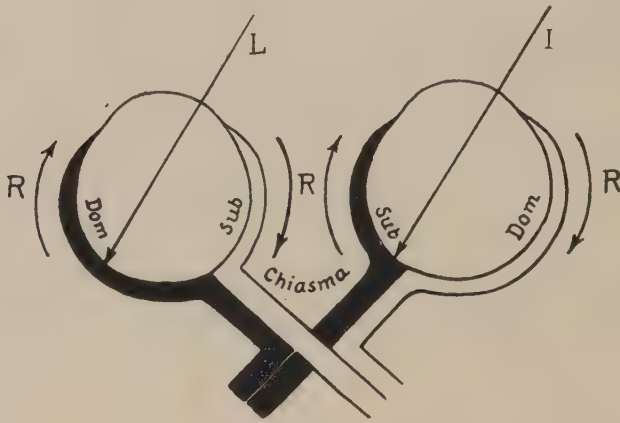


Fig. 3.

Optic motor reactions of the lateral eyes. L.: Ray of light. R.: motor reaction. Dom.: dominant part. Sub.: subordinate part.

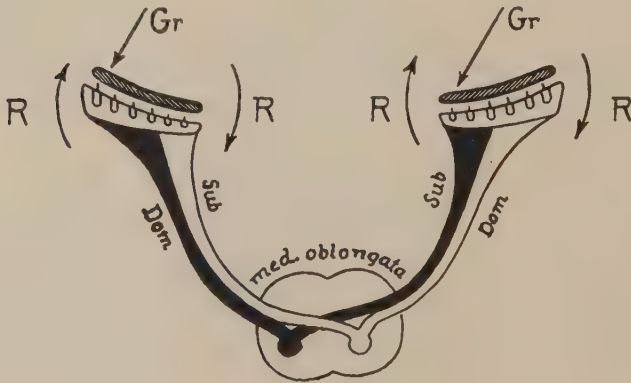


Fig. 4.

Gravitational motor reactions of the utricle. Frontal section. Gr.: Gravitation. R.: motor reaction. Dom.: dominant part. Sub.: subordinate part.

If for instance the pressure of the otolith falls on the outer or the inner part of the macula utriculi (Fig. 4), adequate correctional movements are released. For the sake of complete explanation we have to add the rule of dominance, which says

that the part supplied by the most peripheral part of the fan-shaped expansion of the nerve is the more sensitive. This may often be substantiated by the nervous elements, particularly the sensory cells, being more developed here than in the oppositely situated subordinate part. These rules seem also to apply to the

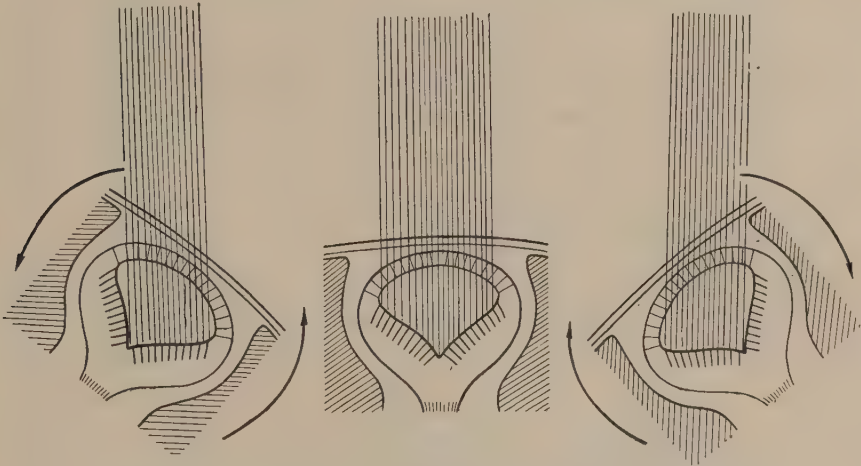


Fig. 5 B.

Fig. 5 A.

Fig. 5 C.

Parietal eye of a lamprey under the influence of light from above. A.: Normal position. B. and C.: Inclination to right and left with supposed optic position regulating motor reflexes.

other sensory organs, *i.e.* skin, lateral organ, and acoustic labyrinth. For further details we refer to our previous works.

If we apply these rules to the parietal eye, we see that it will react to a ray of light falling outside its fovea by a corrective movement which brings the fovea into the ray. As the parietal eye has no muscles—and, according to its development, probably never did have—this corrective movement will bring not only the eye but also the head and the stiff-necked body into a new position (Fig. 5). The ostracoderms lived at the bottom of the water with their body buried and their armoured head just above the mud. All the light would therefore be coming from the zenith in a perpendicular direction. If, then, the position of

the head was altered in relation to the line of gravity, the parietal eye in this way acted as a supplementary static organ.

The modern descendants of the ostracoderms are the hagfish and the lampreys (Fig. 6). The hagfish is a degenerated animal without lateral or parietal eyes and with a much reduced labyrinth. Also the lampreys are in some respects degenerated. But their labyrinth is of the same type as that of the ostracoderms insofar as both types of animals have only two semicircular canals on each side, the horizontal one not yet having developed. Instead, the lampreys have two ciliated endolymphatic sacs, which, as has been suggested by me elsewhere, act as a sort of gyroscope compass, substituting the function of the horizontal canals. No sign of these sacs can be seen in the ostracoderms. We do not know anything about the details of the otolith organs of the ostracoderms, but probably they have resembled those of the lamprey where they are rather different from all higher vertebrates (best description by de Burlet and Versteegh), and perhaps also less efficient. It may be, then that the agnaths (*i.e.* "jawless"), to which class the ostracoderms and lampreys belong—and probably also their prevertebrate forerunners—have been in particular need of a position-regulating supplementary organ.

Such position-regulating optic mechanisms are well known. How they may substitute gravitational mechanisms and behave through the same motor reflexes is seen in experiments on shrimps carried out by Alverdes. If, for instance, both otocysts were removed and also one eye, the animal behaved exactly in the same way as when one otocyst was left in function—or as a vertebrate with one labyrinth. Even in a fish, *Crenolabrus rostratus*, the same positional optic reflex has been demonstrated (v. Holst). If both labyrinths are removed, the animal, in contradistinction to what otherwise happens, is able to keep its usual position. But only as long as the light comes from above. If it is changed to the side of the aquarium the fish will swim on its side with its back towards the light. And if the light comes from below, the animal will turn upside down.

A further study of the anatomy of *Petromyzon* and its larva, the *Ammocoetes*, seems to confirm our hypothesis. As will be seen in Fig. 7 the eye is situated so deeply that its visual field

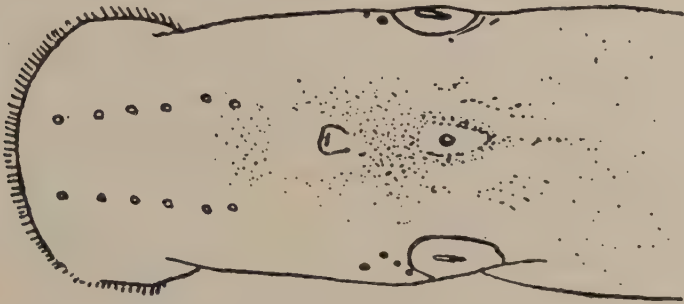


Fig. 6.

Adult *Petromyzon Planeri* (Studnička). The parietal eye with its pigment-free "cornea" seen between the lateral eyes (Studnička).



Fig. 7.

Petromyzon marinus. Sagittal section (Studnička). Po.: parietal eye.
Pp.: paraparietal organ.

is restricted to about 100° . It is, so to speak, a zenith eye. The "lens" is not thicker in the middle and it often shows transverse ridges (Figs. 7, 8, 9). Thus it has no power of refraction. This has been regarded as signs of degeneration. In reality, we believe,

this is of advantage, a proper dioptral system being not only useless to the function suggested above, but even detrimental, as the production and perception of pictures might disturb the perception of light direction. Also the non-spherical, flattened shape of the inside of the eye has been regarded as a sign of degeneration, but in reality it is in accordance with the function suggested.

Most decisive, however, is the shape of the retina, and this is a simple consequence of the particular development of the organ. The retina of the side eyes has developed as an invagination of the neural plate. This forms a vesicle, the top of which becomes the retina. The original surface of the epithelium therefore faces outwards, from the centre of the eye. The eye is "inverted", and the sensitivity of the central part of the retina is not inferior to the periphery, except at the place where the nerve secondarily pierces the retina. The lens is a secondary formation from the outside ectoderm.

The history of the parietal eye is different. It has developed as an invagination of the ependyma of the roof of the interbrain. Also here a vesicle is formed. In this case, however, the top of it constitutes not the retina, but the lens, while the proximal part, the bottom, forms the retina. The surface of the retinal cells consequently faces inwards, towards the centre of the eye. The centre of the retina is formed by the closing (Figs. 9, 10) of the original hollow stalk and therefore becomes the weaker part, probably less sensitive and often with the axis of its cells directed so that they do not coincide with the axis of the dioptral system. The peripheral elements of the retina, on the other hand, seem better developed and situated so that their axis will increasingly coincide with the light rays the more these rays deviate from the dioptral axis (Fig. 11).

It may be added that the increasing height of the lateral parts of the retina, as seen in Fig. 11 and of the forepart in Fig. 8, is in full agreement with our rule of dominance, the dominant part being that supplied by the most peripheral nerve fibres. The

dominance of the forepart of the parietal retina corresponds to the equally pronounced dominance of the forepart of the macula utriculi. In both cases the result is that the upward backward correcting reactions become stronger than the reactions directed

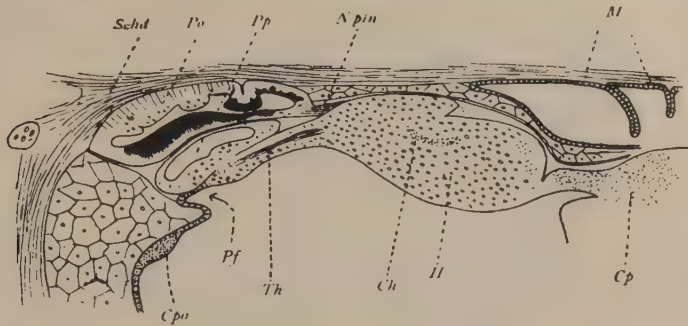


Fig. 8.

Ammocoetes. Late stage. Sagittal section (Studnička). Po.: parietal eye.
Pp.: paraparietal organ. N.pin.: parietal nerve.

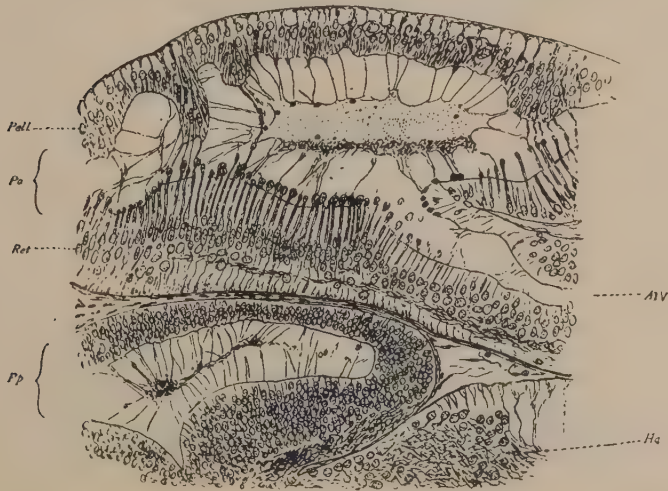


Fig. 9.

Petromyzon fluviatilis. Sagittal section (Studnička). Parietal eye above with "pellucida", corpus vitreum, retina, and communication with the so-called atrium to the right. In the paraparietal organ below a corresponding structure is shown.

upwards and forwards. This is in accordance with the situations to which all individuals are mostly exposed.

We thus see how the parietal eye of the agnaths in every

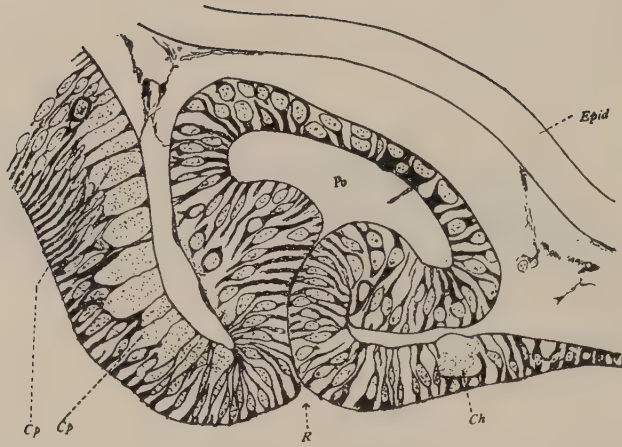


Fig. 10.

Sturgeon. Embryo (Studnička). Formation of the parietal eye by invagination from the roof of the interbrain.

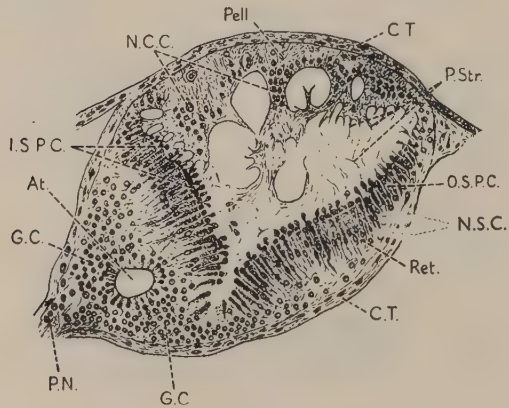


Fig. 11.

Parietal sense-organ of *Geotria*, the New Zealand lamprey. The stage represented is of the sexually immature form, "Velasia Stage" (Dendy). Sagittal section of the right parietal eye (slightly diagrammatic) showing the general structure of the organ. At.: atrium. C.T.: connective tissue. G.C.: ganglion cell. I.S.P.C.: inner segments of pigment cells. N.C.C.: nuclei of columnar cells of pellucida. N.S.C.: nuclei of sense cells. O.S.P.C.: outer segments of pigment cells. P.N.: pineal nerve. P.Str.: protoplasmic strands in interior of vesicle.

Pell.: pellucida. Ret.: retina.

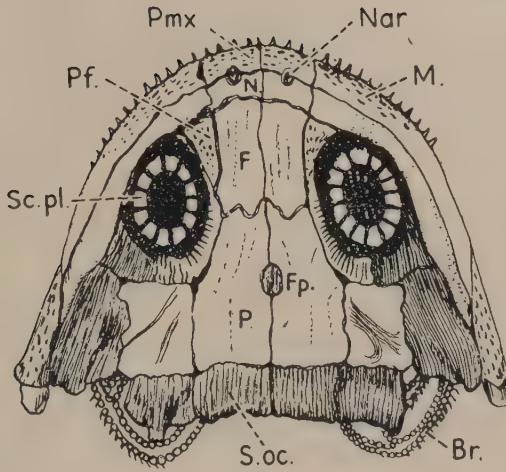


Fig. 12.

Skull of *Protriton* (Gladstone and Wakely).

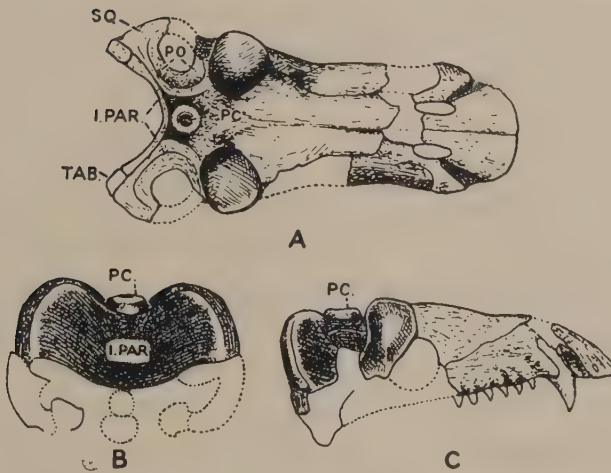


Fig. 13.

Skull of *Titanosuchus* (Gladstone and Wakely). P.C.: parietal foramen.

respect has been fitted to the function suggested. And there is no reason at all to regard it as a degenerated organ. Even those who maintain so, believe that in the lamprey the organ is functioning, that the animal can "see" (Studnička).

While all agnaths (except the blind *Myxine*) seem to have possessed a parietal eye, as seen from their parietal foramen, the organ begins to disappear in the class of fishes. Even if a parietal foramen is found in most of the older extinct forms, we find a solid skull roof already in the very primitive *Dinichthys*, which was a contemporary of the later ostracoderms. In all modern fishes only the most rudimentary stages of a parietal eye are present and the parietal foramen is generally closed. Among the extinct crossopterygians, an older branch, of which the osteolepis is typical, had a parietal foramen, while a later branch, the coelacanth, had none. It is from the older branch that the amphibians are believed to have developed.

It is therefore interesting that in fossil amphibians the parietal foramen and therefore perhaps also the parietal eye has reached its highest development (Fig. 12). Does this mean, then, that the old function has been revived or that a new function has been developed in these only partially aquatic animals?

In modern amphibians the organ has degenerated, so that in the urodeles (salamander- or newt-like forms) it has practically disappeared, and in the anures (frogs and toads) it has been reduced so that only a little vesicle without pigment and without nerve, lying outside the skull, is left.

In the class of reptiles the organ is found, not only in fossil, but also in modern species. It is found even in the sidebranch from which the mammals have developed, as illustrated by the large carnivorous mammal-like *Titanosuchus* (Fig. 13), where the diameter of the parietal foramen reached 1 cm. It was a very primitive form that lived in the Perm period about 100 million of years ago. In the archisauroids many of which had a bipedal gait and to which belong the dinosaurs and the crocodiles and from which developed the comparatively late birds, the parietal eye

was absent. This is also the case in the rather primitive turtles and their ancestors. It may perhaps have something to do with their heavy armour and their habit of hiding their head under their shield. The rynchocephalians had a parietal foramen and their modern representative, the "living fossil" the tuatara (*Sphenodon* or *Hatteria*) has a well-developed parietal eye. This also applies to many living saurians. It is not easy to find any correspondence between the possession of a well developed parietal eye and the way of living. The fact that the rather primitive geckos have no parietal eye, may, however, have something to do with their nocturnal life. The still more primitive *Sphenodon* is comparatively lively, but mainly at night. The saurians are the liveliest of the reptiles. In the rather sluggish *Chamaeleo* the parietal eye is poorly developed. The lizards have a well-developed eye. In the serpents, a comparatively late side-branch of the saurians, the organ is absent.

If we examine the structure of the parietal eye of modern reptiles we again meet with features which hitherto have been regarded as signs of degeneration, but which in our opinion, only serve to prevent the forming of pictures on the retina. The inside of the parietal eye is hardly ever spherical as is the case with the lateral eyes. In most cases it is flat as in *Iguana tuberculata* (Fig. 14), in the embryo of the blindworm, *Anguis fragilis* (Fig. 15) or in the big monitor, *Varanus giganteus* (Fig. 16). In other cases the eye cavity is deep as in *Anolis*, another iguana (Fig. 17) and in *Sphenodon* (Fig. 18).

Other factors disturbing a proper dioptral system are the shapes of the retina and the lens. The retina may be bulging in the middle as in the *seudopus* and the *Leiolaemus nitidus* or it may be funnel-shaped as in the *Sphenodon* (Fig. 18). The *Varanus giganteus* (Fig. 16) has a medium notch on the back of the lens. In the same animal the lens, moreover, has a considerable aggregation of pigment in the middle. This is also the case in other saurians as *Anguis fragilis* (Fig. 15) and *Anolis* (Fig. 17). But the form of the lens is always such that a refraction of light

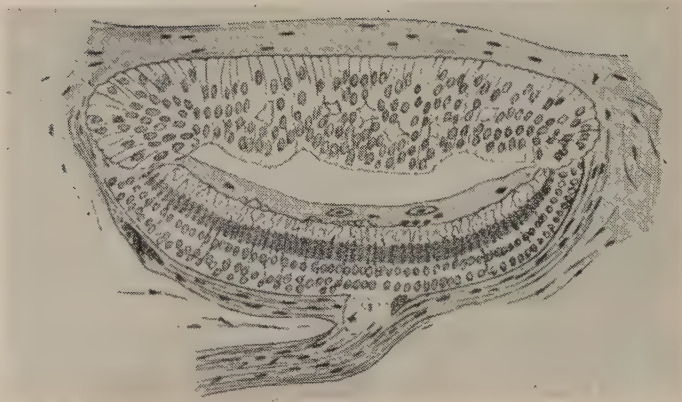


Fig. 14.

Iguana tuberculata. Adult (de Klinckowstroem from Studnička).

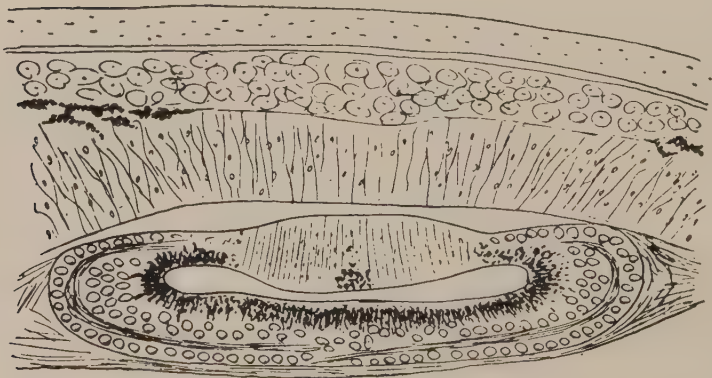


Fig. 15.

Blindworm (*Anguis fragilis*). Embryo (Béraneck from Studnička).

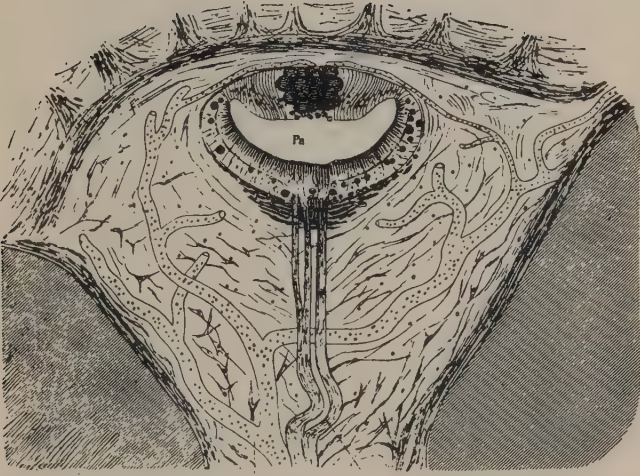


Fig. 16.

Monitor (*Varanus giganteus*) (Spencer).

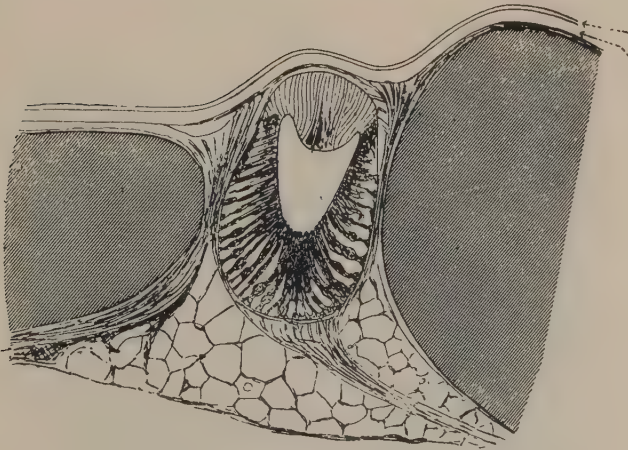


Fig. 17.

Anolis (Spencer).



Fig. 18.
Sphenodon (Dendy).

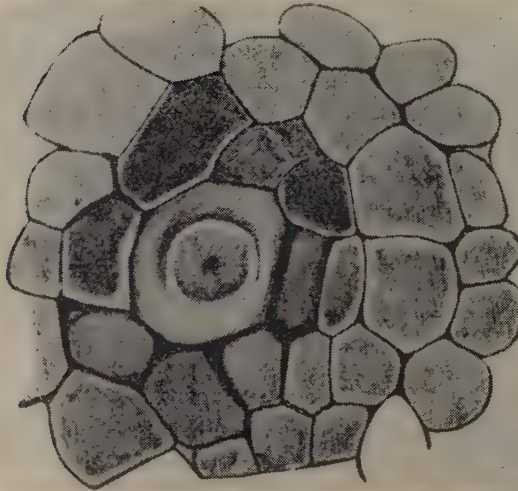


Fig. 19.
Varanus giganteus. The parietal eye is seen through the transparent cornea (Spencer).

will take place. When the unusual shape of the dioptral system has been regarded as a result of degeneration, it must be remembered that the degenerated lateral eyes in the blind *Proteus* have retained their spherical shape (Semper). All their elements, on the other hand, are far more reduced, than in the saurian parietal eye.

The only valid sign of a rudimentary condition is the degeneration of the parietal nerve. In many of these animals the nerve is more or less degenerated or altogether wanting, at least in fully developed individuals. In several of the older publications the description as to this point is not quite clear. The very reliable investigator, Studnička, declares, however, that in the lizard, *Lacerta agilis*, it is possible, also in adults, to follow the nerve fibres from the eye to the brain¹. Also in *Varanus* the nerve fibres seem to be preserved (Spencer). Both animals have a well-defined transparent cornea (Fig. 19). This is also the case in the *Calotes ophiomachus* and in the *Iguana tuberculata*. In the former no information regarding the nerve exists and in the latter the nerve has been described as existing only in embryos. In *Anolis* the nerve fibres have been regarded as wanting by Studnička and Gladstone and Wakely on account of an incomplete illustration of Spencer. In *Sphenodon* the nerve fibres seem to exist in the embryonic as well as in the postembryonic stage (Dendy). Gladstone and Wakely report, that this also was found by Schauinsland. This author, however, seems to have examined only embryos.

Also in reptiles we therefore must suppose that the parietal eye in some cases is still a functioning organ, although its degeneration in other cases is in rapid progress.

The posterior organ, the epiphysis, is also greatly reduced in many saurians and in turtles. It is fairly developed in serpents, which have no parietal eye. In crocodils both the anterior organ

¹ I could not, however, find any trace of the nerve in serial sections of an adult specimen of *Lacerta viridis*, put at my disposal by the courtesy of Professor Adrian Cappers, Groningen.

(the parietal eye) and the posterior organ (the epiphysis) are completely missing. In birds and in mammals only the epiphysis is left in the shape of a glandular organ. A corresponding transformation of the parietal eye is seen in bony fishes.

But what is the function of the parietal eye in reptiles and probably also in extinct amphibians? It cannot have anything to do with aquatic life and static orientation as is the case in agnaths and in primitive fishes. A sun compass function as found in insects is also out of the question. The shape and detailed structure is not fitted to a function of such precision. It is also made impossible by the flexibility of the neck in the animals concerned. I have not been able to solve this problem, but in a discussion with the zoologist Weiss Fogh, he has suggested that the reptilian parietal eye becomes stimulated by light, and that this stimulus in some way or other acts on an endocrine process. And this brings us back to Rabl-Rüchard, who in 1886 maintained that the function of the parietal eye was to estimate the heat of the sun's rays, and that it was a thermal sense organ rather than a visual one. He suggested that the purpose of the organ was to warn the animal against the noxious influence of the tropical sun. At a later stage of development the sensory organ degenerates and is changed into a secretory organ, a development which has other parallels. In locusts, for instance, the forehead is provided with sensory hair cells, which when stimulated by a current of hot air produce a reaction that make the locust fly directly against this wind. In some relative species this sensory apparatus has degenerated to a glandular organ (Weiss Fogh). Secretory and sensory cells are known to be closely related. The vitreous body in the *Sphenodon* is believed to be a secretory product of the lens (Dendy, postscript) or of the lens as well as of the retina (Nowikoff). What sort of internal secretion is connected with the parietal eye we cannot say. Light by direct action on the human skin produces a formation and a migration of pigment (also seen in certain reptiles) and has a beneficial influence on the whole body, probably due to

a generally increased flow in the capillaries. In the frog, besides, a migration of retinal pigment takes place, also when the eyes are not directly exposed. Would it be possible that the concentrated light in a somewhat similar manner could act even on a nerveless parietal eye and set substances free which by way of the surrounding vessels, and perhaps through their nerves, might have further reaching effects?

If we cannot tell for certain what has been the function of the parietal eye in reptiles and amphibians we may perhaps suggest at least some of the causes which have made it disappear. With the development of the hemisphere of the brain, the parietal organ necessarily is pushed from the top to the back of the head and the zenith gets out of its axis, a fact which renders it useless. The development of powerful jaws has made the temporal muscles increase, which often has given rise to a parietal crest. In this way the parietal foramen is closed. In the case of the *Titanosuchus* referred to above, Fig. 13, nature seems to have tried to prevent the "drowning" of the parietal eye between the large temporal muscles by building a vertical periscope-like osseous funnel. To these causes, which previously have been discussed, it may be added that the parietal eye of the reptiles probably has kept some of its position-regulating qualities. The impulses resulting from this must of course be misleading so that the value of the organ is reduced and it then disappears.

It should be possible to test the validity of the above hypothesis by experiments. In lamprey one might establish the motor reactions under various combinations of elimination of side eyes, parietal eye, and labyrinth in various positions. The same might be done in suitable reptiles under varying direction, intensity, and duration of irradiation. Action currents may be measured.

But all this is outside the scope of the author, who feels that he already has surpassed his proper domain by this, to him, so tempting digression.

CONCLUSIONS

Certain features of the parietal eye: the non-spherical shape of the dioptral system, peculiar shape of the lens and retina, and aggregation of pigment in the lens have hitherto been regarded as signs of degeneration, but are only devices to prevent a proper picture-building and perceiving.

In accordance with its special development the parietal eye was never destined for sight in the same way as are the lateral eyes.

In agnaths—ostracoderms and living lampreys—and in extinct fishes the parietal eye seems to be a position-regulating supplementary static organ.

In reptiles and perhaps in extinct amphibians the parietal eye probably perceives light intensity. This stimulation influences an unknown process, perhaps of internal secretion.

In lampreys and certain reptiles the organ must be supposed to be still in complete function.

POSTSCRIPT

Accelerations and altering of head posture give rise, as we know, to compensatory motor reactions of the lateral eyes. The parietal eye is immoveable. If the parietal eye were a real visual picture producing organ, the result of the said movements would be two systems of non-corresponding visual fields and consequently a confusing visual perception. This seems to prove that the parietal eye cannot be a real visual organ.

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Contribution to the Surgical Treatment of Inoperable Tumours Causing Obstruction of the Sylvian Aqueduct

By

GÖSTA NORLÉN, M.D.

During recent years, the surgical treatment of inoperable tumours of the brain stem causing obstructive hydrocephalus has roused interest, especially after Torkildsen introduced his procedure of draining the lateral ventricle into the cisterna magna by means of a rubber tube. He has shown that tumours in the posterior part of the third ventricle and the brain stem have an extremely moderate expanding activity, and that the patient can live for many years if only the hydrocephalus can be drained. Good results with this method have also been reported by several authors, and in our material one patient with an inoperable tumour at the bottom of the fourth ventricle is still living and is in good condition 10 years after insertion of the rubber tube.

About 5 years ago Leksell, at the Neurosurgical Clinic, Stockholm, introduced a new method in the treatment of atresia of the Sylvian aqueduct. In preceding years, when temporary aqueductal drainage was used in the treatment of stenosis of the aqueduct, it was found that catheterization of the aqueduct carried very little risk in itself and was usually easily performed. Now Leksell, after catheterization with a soft rubber catheter, introduced a spiral of thin metal wire, which was then per-

manently left in the aqueduct, thus obtaining a reconstruction of the aqueduct.

In the following two cases, on exploration of the fourth ventricle, a small astrocytoma was found in or near the aqueduct causing an occlusion. In both cases it was possible to insert one of these metal spirals into the aqueduct and obtain a pas-

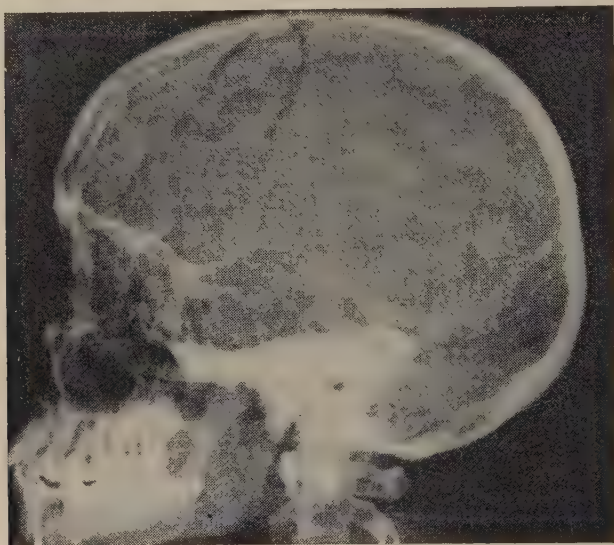


Fig. 1.

sage between the third and fourth ventricles. The good results after about two years observation speak in favour of this method being tried out in similar cases.

Case 1. Serafimerlasarettet 1044/48, female, clerk, age 17 years.

1942 tuberculosis of the lungs with very slight changes. Was treated 4 months in hospital.

Present illness started in the beginning of 1946 with headache. In August 1946 slight gait disturbances with dizziness and slight clumsiness in the right hand. Choked discs were found in December 1946 and the patient was referred to the Neurosurgical Clinic with a suspected cerebellar tumour.

Examination. Choked discs 2-3 diopters. Nystagmus. Diadochokinesis of the right hand. Positive Romberg's sign. Unsteady gait.

X-ray examination. Pronounced signs of increased intracranial pressure with dilatation of the sutures and marked impressiones digitatae. Widening of the sella turcica and destruction of the dorsum of the sella (Fig. 1).

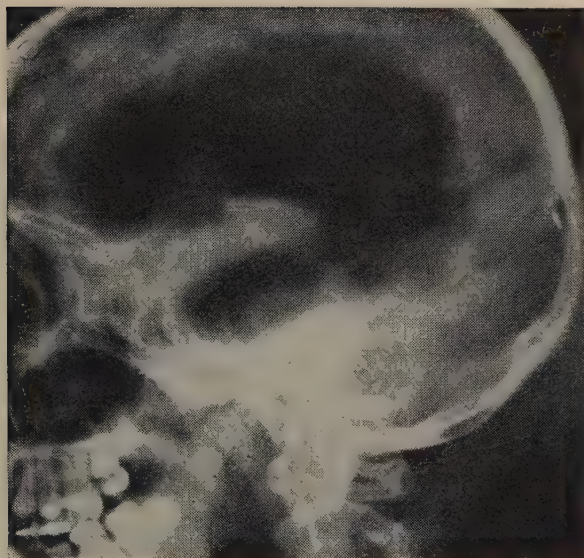


Fig. 2 a.

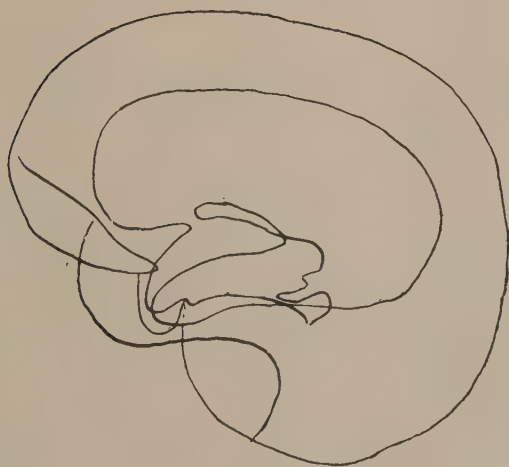


Fig. 2 b.

Ventriculography. Pronounced hydrocephalus with dilatation of both the lateral and third ventricles. The aqueduct was displaced backwards and upwards. Only the most proximal part of the fourth ventricle, close to the aqueduct, was filled with air. The ventriculographic diagnosis was expanding lesion in the posterior fossa causing an obstruction of the fourth ventricle (Fig. 2-a and b).

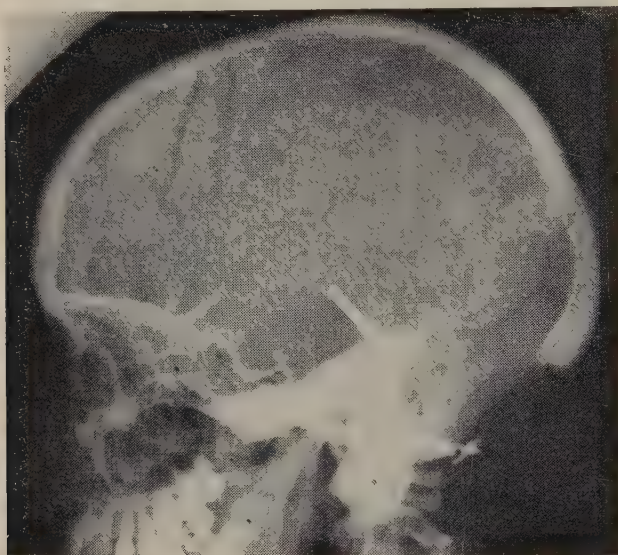


Fig. 3.

Operation (Jan. 2nd, 1947). A small astrocytoma was found in the most cranial part of the bottom of the fourth ventricle, a little to the right, close to the orifice of the aqueduct, and compressing it. A small piece of the tumour was excised for examination. It was possible to catheterize the aqueduct with a rubber catheter and a spiral of thin metal wire was then introduced and left in place, thus causing a communication between the 3rd and 4th ventricles.

Postoperative course. The first few days after the operation, the patient was very drowsy but gradually improved. A dye test 3 weeks after operation showed that communication had been established, and the patient left the hospital. In an other hospital she received a series of X-ray treatments.

She was again examined in the hospital in May 1949. A marked improvement had occurred. There was no headache, and the clumsiness in the right hand had disappeared. A slight disturbance of gait was the only symptom left. The eye grounds were now normal, no nystagmus. Very slight adiadochokinesis of the right hand. Romberg's sign was still positive.

X-ray examination. Since the last examination there had been a recalcification of the sella turcica and it now looked quite normal. The widening of the

sutures had disappeared and the impressiones digitatae were not so pronounced (Fig. 3).

Ventriculography. On puncture of the lateral ventricles there were no signs of increased pressure. The hydrocephalus had diminished considerably. The metal spiral was still in position, and air passed through the spiral aqueduct into the fourth ventricle (Fig. 4).

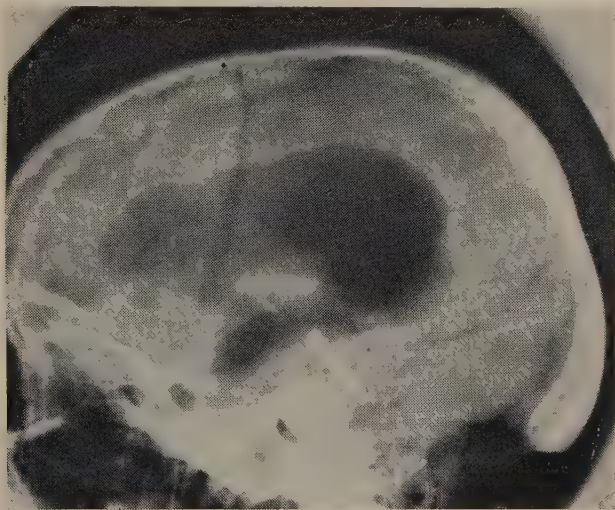


Fig. 4.

Comment: In this case of an inoperable tumour high up in the 4th ventricle with occlusion of the aqueduct, it has been possible to achieve a reconstruction of the aqueduct with a spiral of thin metal wire. On examination more than two years after the operation a pronounced improvement had occurred of both subjective and objective symptoms. The choking of the discs had disappeared as also the roentgenological signs of increased intracranial pressure. The hydrocephalus had diminished. The metal spiral was still in its original position and air passed through it into the 4th ventricle and the cisterna magna.

Case 2. Serafimerlasarettet 765/47, school-girl, age 13 years.

Present illness started in 1945 with headache combined with nausea and vomiting. Sometimes blurred vision. Lately the headaches had increased in severity.

Examination. Choked discs of 5 diopters bilaterally. No other neurological signs.

X-ray examination. Pronounced signs of increased intracranial pressure with decalcification of the sella turcica (Fig. 5).

Ventriculography. Pronounced hydrocephalus including the third ventricle. The aqueduct was filled with air about 1 cm. from the 3rd ventricle. It was slightly dilated and its most distal part widened (Fig. 6 a and b).

Operation (Oct. 10th, 1947). A small astrocytoma was found just in the mouth

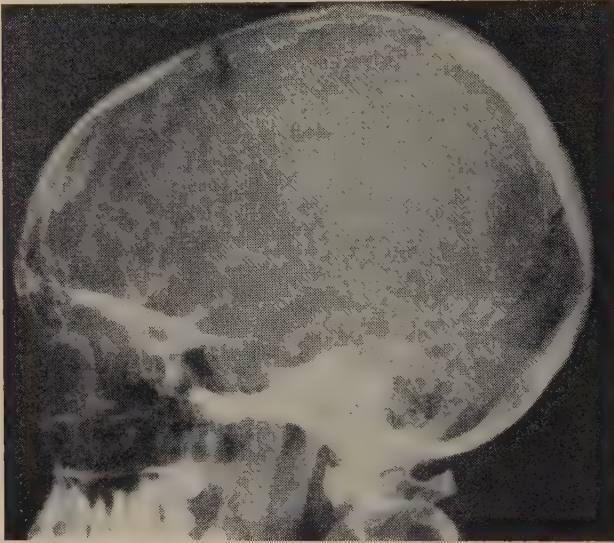


Fig. 5.

of the aqueduct leading into the 4th ventricle. A small piece of the tumour was removed with a forceps. It was then possible to introduce a rubber catheter with a metal spiral into the aqueduct, and after removing the catheter, leave the metal spiral, thus establishing a communication between the 3rd and 4th ventricles.

Postoperative course. Slight temperature and vomiting the first days. A dye test 3 weeks later showed no communication, and on X-ray the position of the spiral was thought to be a little too high (Fig. 7).

A *reexploration* of the fourth ventricle was made which showed, however, that the inferior end of the spiral was situated in the fourth ventricle and that liquor was passing through it.

After this second operation an insufficiency of the muscle sutures appeared. A resuture had to be done. The postoperative course was then uncomplicated, and the patient left hospital on Nov. 11.

In February 1949, the patient was in excellent condition. There were no subjective symptoms. She had started school in August 1948 and was doing very well.

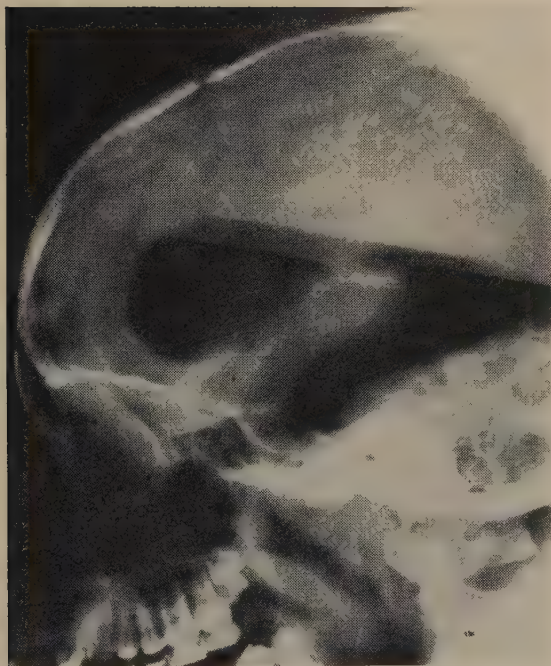


Fig. 6 a.

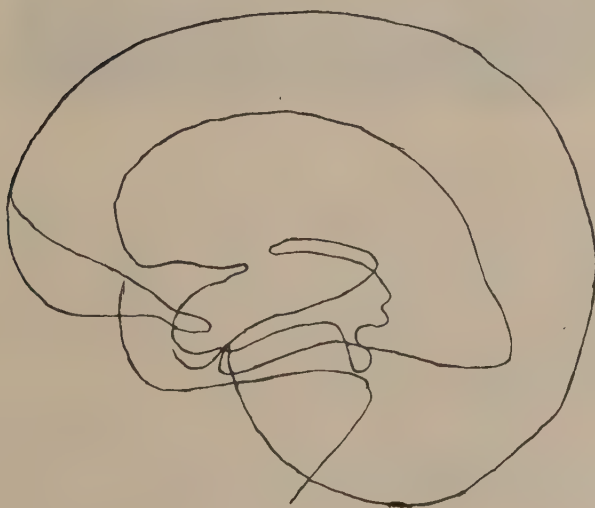


Fig. 6 b.

Comment: In this case a new ventriculogram was not performed, but the marked improvement speaks in favour of a reconstruction of the aqueduct having been achieved by the metal spiral.

It is beyond the scope of this paper to discuss all the details in the differential diagnosis of an atresia of the Sylvian aqueduct

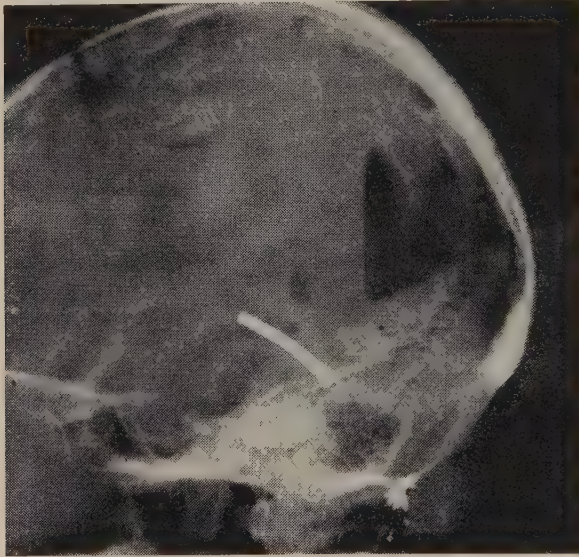


Fig. 7.

and a tumour causing occlusion of the aqueduct. Already in 1935 Lysholm had described the funnel-like appearance of the proximal part of the aqueduct in stenosis. In cases of tumours, the aqueduct is usually dilated with a widening of its most distal end as seen in the two cases described above.

Hyndman (1938) observed that a combination of ventriculography and encephalography after an injection into the sub-arachnoidal space might be of great value in certain cases. In a case of atresia of the aqueduct of Sylvius operated on by the author, this combined examination was performed by Lindgren at the Roentgenological Department of the Seraphimerlasarettet.

The case was reported by him in 1949. Ventriculography suggested that the occlusion was of inflammatory origin and not caused by a tumour. From a correlation with the encephalographic finding, which showed the air outlining the quadrigeminal plate and the pons, it was definitely established that no expanding process could be present at the level of the stenosis. In cases of suspected obstructive lesion of the aqueduct, this combined examination appears to be of great value in giving information about the true nature of the lesion. We think it advisable to start with the encephalography as this examination causes less discomfort to the patient.

SUMMARY

1. In cases of inoperable tumours causing obstruction of the Sylvian aqueduct, it has been possible to perform a reconstruction of the aqueduct by means of a spiral of thin metal wire. Two cases are reported, both living and in good condition about two years after operation.

2. The combined examination of encephalography and ventriculography is recommended in cases of suspected obstructive lesions in or near the aqueduct of Sylvius.

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Cholesteatomas of the Cerebello-Pontine Angle

By

H. OLIVECRONA

The cholesteatomas are rare tumors, only 29 cases having been verified in this clinic up to March 15, 1949. The following locations were observed (Table I).

Location	No. of cases
Cranial vault (in the bone)	3
Suprasellar	6
Base of brain (Supratentorial)	4
Sylvian fissure, temporal lobe	3
Intraventricular	6
Cerebellopontine angle	7

29

One cholesteatoma was found in the fourth ventricle, otherwise all posterior fossa tumors were located in the angle. Since about 50 % of the angle tumors give rise to a typical syndrome a report of our cases seemed worth while.

CASE REPORTS

Case no. 1. Neurosurgical Clinic 668/37. K. C. male 24 years. For seven years typical trigeminal neuralgia affecting the third branch of the right side. Several alcohol injections with temporary relief. Admitted nov. 18, 1937. Neurological examination was entirely negative, the corneal reflex was normal on both sides. Röntgenological examination of the porus showed nothing abnormal. A diagnosis of cholesteatoma was made. Operation nov. 23, 1937. A

small cholesteatoma between the 5th and VIIIth nerve was found and removed. Two thirds of the sensory trigeminal root were divided, resulting in a moderate hypaesthesia in the right trigeminal area, most marked in the third division. In his last report dated March 1948 the patient states that since the operation he has been entirely well.

Case no. 2. Neurosurgical Clinic 703/37. E. B. female 29 years. Since four years typical trigeminal neuralgia affecting the third branch on the left side. Admitted to the clinic dec. 8, 1937. Neurological examination showed entirely normal conditions. A diagnosis of cholesteatoma of the angle was made. Operation dec. 12, 1937. A small cholesteatoma was found between the 5th and VIIIth nerves. The trigeminal root was dislocated backwards. The tumor was removed and half the trigeminal root divided. The sensory loss was insignificant. In her last report dated July 1946, the patient reports herself well.

Case no. 3. Neurosurgical Clinic 319/38. R. J. male 32 years. Since 6 years trigeminal neuralgia affecting the third branch on the left side. During the last few months the pain has been spreading also to the second division. Temporary relief after alcoholinjection of the third branch. Admitted May 2, 1938. Aside from slight hypaesthesia of the third trigeminal division on the left side following previous alcohol injection neurological examination was negative. A diagnosis of cholesteatoma of the angle was made. At operation on May 6 a cholesteatoma the size of a walnut was removed. At the same time tractotomy was carried out resulting in almost complete analgesia of the left trigeminal area with loss of the corneal reflex. In his last report dated April 1946 the patient states that since his operation he has been entirely well.

Case no. 4. Neurosurgical Clinic 148/48. G. H. female 22 years. Since one year trigeminal neuralgia affecting the third branch of the right side. There was a distinct diminution of the corneal reflex on the right, otherwise neurological examination was negative. A lumbar encephalogram was made showing that the cisterna pontis on the right side was dislocated in a lateral direction. The cistern was considerably smaller than on the other side. The cisterna ambiens on the right was dislocated in an upward direction (Fig. 1). At operation on March 12, 1948 a cholesteatoma, the size of a walnut, was found between the 5th and VIIIth nerves, compressing the fifth nerve and dislocating it in a dorsal direction. The tumor was removed and the trigeminal root divided. The patient left the hospital two weeks later, free from pain. There was complete anaesthesia of the right side of the face.

The clinical picture in all these cases was very uniform. Trigeminal neuralgia affecting the third division in young people, all very much below the average age of the ordinary tic douloureux. The average age at onset was 23 years. Neurological defects

were lacking, except for a diminished corneal reflex in one case. The trigeminal neuralgia except for the preference for the third branch and the age of the patients showed nothing to distinguish it from the ordinary tic douloureux.

Among the remaining three cases two presented an advanced

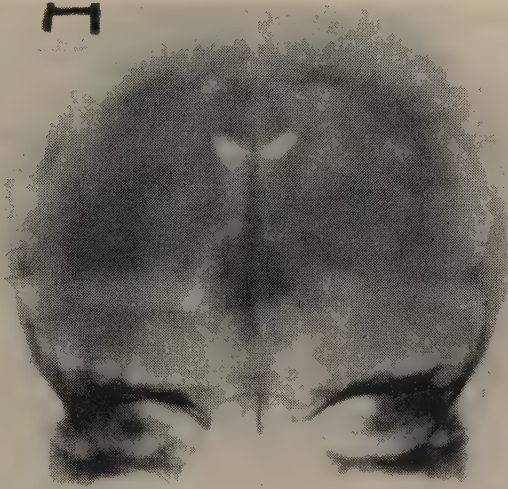


Fig. 1.

Case no. 4. Encephalogram shows dislocation of cisterna pontis in the lateral and of the cisterna ambiens in the cranial direction.

though somewhat atypical angle syndrome and one a general pressure syndrome without localizing symptoms.

The relative frequency of trigeminal neuralgia in cholesteatomas of the cerebellopontine angle has been commented upon by several authors. Mahoney (1) found trigeminal neuralgia in 25 % of the 53 parapontine tumors assembled by him from the literature but since a considerable part of this material consisted of inveterate cases, often without detailed clinical histories, the real frequency might actually be greater. In Tönnis (2) 6 cases trigeminal neuralgia was an outstanding symptom in three. Dandy (3) also mentions the frequency of trigeminal neuralgia in his cases.

Trigeminal neuralgia also occurs in other tumors of the angle but is comparatively rare. In the neurinomas of the eighth nerve trigeminal neuralgia is observed in a few per cent of the cases, in the meningiomas trigeminal pain is somewhat more frequent but still a rare phenomenon. These tumors, especially the neurinomas usually cause a number of other symptoms, some of them, such as an enlarged porus (present in over 80 % of the cases), pathognomonic, and the problem of differentiation against a cholesteatoma of the angle therefore seldom arises. Small meningiomas may be impossible to distinguish from cholesteatomas and the same may be said about arteriovenous aneurysms in this location. These latter tumors are very rare, however, but one of the three cases seen in this clinic presented a trigeminal neuralgia of the third branch as the principal symptom and a cholesteatoma was actually suspected in this case.

The differential diagnosis against a true trigeminal neuralgia may be definitely settled by means of an encephalogram made according to the technique proposed by Lindgren (4). Dislocation of the cisterna pontis and the cisterna ambiens definitely proves the existence of a tumor in the angle and indicates exploration of the trigeminal root by the posterior route. As more room will be needed when a tumor is present it is advisable to make the bone defect larger than is customary in an ordinary root section.

The contents of the tumor are usually easily removed but the capsule may be adherent to the basilar artery and other important vascular structures. From our experience with cholesteatomas in this and other locations it may be concluded that recurrences are rare even if most of the capsule is left behind and in view of the catastrophic complications which may arise if some important artery is torn in an attempt to remove the capsule completely our policy has been to remove only such parts of the capsule as come away easily. So far there have been no recurrences among the angle tumors although most of them have been under observation for 10 years or more. Should a recurrence

occur, which has happened twice in our supratentorial cholesteatomas, the recurring tumor may easily be removed.

It would probably be quite safe to leave the trigeminal root intact as it is adequately decompressed by removing the contents of the tumor. However, for reasons of safety we have divided the root partially in two cases with insignificant sensory loss and completely in one case. In one case tractotomy was done with good analgesia of the affected side. The pain was completely relieved in all cases and has not recurred. Dandy (5) also feels that the root should be divided but it is probably quite sufficient to divide the posterior half of the root and thus save the patient from the inconvenience of a complete anaesthesia of the corresponding trigeminal area.

SUMMARY

In cholesteatomas of the cerebellopontine angle a typical syndrome may be observed consisting of:

- 1) A typical trigeminal neuralgia in a young person, usually in the age between 20-30, affecting, or at least beginning in the third branch, with or without loss of the corneal reflex.
- 2) Absence of Roentgenological changes of the skull and particularly of the porus.
- 3) Absence of neurological defects excepting the fifth nerve.
- 4) Dislocation of the cisterna pontis and the cisterna ambiens in the encephalogram made according to the method of Lindgren.

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Constriction Ring Dystocia

By

DAN PRYTZ, M.D.

A definite constriction ring dystocia is rather a rare, but very serious obstacle to parturition, which may require difficult and often mutilating intervention, with a certain amount of risk to the mother as well¹. Ordinarily, only quite definite and severe cases are diagnosed. *Gammeltoft*, for instance, found constriction ring dystocia in 23 of 35,000 parturitions (0.07 per cent.). *Rucker*, with especial attention directed toward constriction ring dystocia, found this complication in 1.67 per cent. of his last 10,000 parturitions.

The constriction ring consists of a circular, spasmodic uterine contraction, which is apparent on the surface of the uterus as a transverse band. It is presumed to be a phenomenon of fatigue similar to the tetanic spasms which may occur in other muscles following excessive use. It will be found more frequently in cases of the less common fetal positions, in women with pelvic constriction, primipara in older persons and also in connection with excessive use of labour-stimulating medications. *Gammeltoft* mentions three main causes of constriction ring dystocia: (1) early discharge of the liquor amnii, (2) intra-uterine manipulations, (3) irregular, painful contractions of the uterus. It cannot be left out of consideration, that the use of any uterine stimulant may be a causative factor in constriction ring dystocia.

¹ "C'est une complication presque sûrement mortelle au fœtus et qui peut amener pour la mère plus grands dangers". (*Leop. Meyer*, 1910).

The clinical picture of a constriction ring dystocia is protracted labour, with no other reasons being evident by ordinary examination. Even digital vaginal exploration will, as a rule, give no clue, unless the possibility is kept in mind. By examination during labour it may, however, be noticed that the cervix is relaxed and that the presenting fetal part exerts no pressure against the orifice. The contractions are, as always in protracted births, somewhat fluctuating, often quite painful, although the general picture shows nothing characteristic. At times the constricting band across the uterus may be observed directly through the abdominal wall. A definite diagnosis is established only by manual vaginal examination. The ring may then be felt as a marked, frequently rigid ridge, closing tight around the fetus. It will, as a rule, be localized to the area around the internal orifice, but may be found higher.

Fetal mortality has until lately been high, often given at about 85 per cent. These statistics, however, include only well advanced, severe cases. During these 10 to 20 years mortality has been considerably reduced in many places. *Rucker*, e.g., gives a fetal mortality of 18 per cent. *H. Johnson* has even reached only 5 per cent. This is hardly due primarily to consistently conservative treatment, as has been recently stated. Rather, the improved prognosis is accounted for by the inclusion of relatively less severe cases in recent reports, and more especially by the treatment used during recent years, a combination of antispasmodics and active therapy. The antispasmodics produces a frequently brief, temporarily favourable, condition for the delivery.

Conservative treatment is indicated in those rarer cases of constriction ring dystocia, where the orifice is not passable to the fetus. It consists of large doses of morphine, building up the patient's general condition by adequate amounts of nutrients, salt and fluids, and control of the imminent or already developed infection. Often, however, active intervention becomes necessary in the end.

For active therapy, under protection of preceding treatment with antispasmodics, various substances may be used. Relaxation of the constriction ring is seldom achieved by even deep anesthesia alone. A better antispasmodic effect is obtained by amyl nitrite inhalation (3 cgm), magnesium sulphate (1 gm i.v.) and epinephrine ($1\frac{1}{2}$ -1 mgm i.m.). *Rucker* reports a fetal mortality of 18 per cent after the introduction of epinephrine treatment. On the whole, epinephrine and magnesium sulphate seem to be the preferred remedies in America.

Three authoritative works about amyl nitrite treatment in cases of constriction ring dystocia have been published in Denmark. All three works give convincing evidence of the good effect of amyl nitrite treatment, which here, as well as in England, where it originated, seems to be the one most generally accepted. Treatment by amyl nitrite inhalation as a preparation for delivery in cases of constriction ring was introduced by *W. Gilliat*. *R. Barnes*, however, as early as 1876 stated that amyl nitrite is an uterine relaxing agent. *F. Barnes* in 1882 used amyl nitrite before removing placenta in a case of hour-glass contraction of uterus during the third stage. *Soutar* in 1906 used amyl nitrite as an 'antidote to the chloroforme' in delivery at a case of transverse presentation and constriction ring dystocia. *Gilliat*, *Croft*, and others state that the treatment by amyl nitrite in nearly all cases of constriction ring dystocia proved highly effective. *Gilliat* himself reports only one case in which it was unsuccessful.

The treatment is simple, easily administered, inexpensive, and, as a rule, without danger. Contraindications are very rare (glaucoma, severe circulatory disturbances, especially shock). Effects are quite brief, so that atony and later bleeding is seen no more frequently after this treatment than otherwise.

At the Amtssygehus in Haderslev we have during the past 27 years had a total of 3200 parturitions; of these 900 pathological, 5 of them cases of constriction ring dystocia. One of these five patients had an external conjugate of 17 cm, one showed a

posterior rotation of the occiput, otherwise no abnormalities were found beyond the constriction ring. All five patients had, because of protracted labour, received labour-stimulating injections, two of the women morphia as well. The first four patients were para I, the oldest being 36 years. For two of these labour was terminated by embryotomy during deep anesthesia after respectively 3 and $3\frac{1}{2}$ days vain labour efforts, during which time the fetuses died. These weighed 3000 and 3100 gms. The other two parturitions were completed by forceps during deep anesthesia, one of them preceded by digital dilatation of the constricting ring. Both labours lasted about $2\frac{1}{2}$ days. The babies weighed 2900 and 2950 gm, they were asphyxiated at birth, but were discharged in good condition. Puerperium was normal for two of the mothers, feverish for two, protracted (3 wks.) for one of these.

The fifth case at Haderslev Amtssygehus I treated personally, and I chose to attempt active therapy under protection of amyl nitrite treatment. This case of a typical well-developed constriction ring at a para II was a multiple birth (twins), details of which follow. Amyl nitrite treatment was highly effective, so that the following forceps delivery was mere child's play.

Case report: The patient was a 32 yr. old para II. The first parturition and puerperium normal. After a normal pregnancy with twins the patient began labour at full term, shortly after the rupture of the membranes at 3.20 o'clock. At 8 o'clock a live girl, 2600 gm, 48 cm, was born. Half an hour later pains again became stronger. When, $2\frac{1}{2}$ hrs. later, there was still no progress, despite good contractions, a physician was called. He made a vaginal examination, ruptured the membranes and made a replacement of two forelying hands. When there was still no progress, and contractions had diminished, the patient was taken on an automobile trip over rough roads—with no effect. Later pituitrin (0.2-0.4 cc) was administered every half hour for three doses, whereupon contractions increased. But when the fetus was still high and had not moved at all 12 hrs. after birth of the first twin, the patient was brought to the hospital.

On admission some adipositas was found. Fetal position L. O. P., the head fairly engaged in the pelvic entrance. *Mc. Donald's* measure 39 cm. Fetal size was judged to be not over 3500 gm. Fetal heart-sounds normal. 7-8 cm above symphysis a transverse furrow which was partly obliterated by catheterization

(350 cc normal urine). Rectal examination revealed the head high, unrotated, just as the attending physician had found all day. The cervix was almost dilated. No small parts could be felt. Contractions were quite good. With still no signs of progress an hour and a half later, vaginal examination was done, which revealed nothing new. Pituitrin, 0.2 and 0.3 cc, was given a half-hour interval. Still no progress. The furrow above symphysis was now more pronounced, located perhaps a trifle higher. Slightly more than fifteen hours after the birth of the first twin manual vaginal examination verified the diagnosis of constriction ring, which was felt as a finger-thick, circular ridge around the neck of the fetus. It was just possible to pass a finger through the ring, which felt tense, somewhat rigid, but not hard.

Under ether anesthesia (Wanschler's mask) forceps were applied (the Copenhagen Birth Institute's model) to the high-situated, unrotated head, so that the forceps of necessity had to be placed over forehead and occiput. The ether bag was removed and on an open mask 30 drops of 'solutio amylii nitritis pro inhalatione' (6 cgm. amyl nitrite) were dripped fairly rapidly. A pull on the forceps, and a moment later the head began to descend; and by one moderate traction delivery was accomplished in about a minute. A boy, 3350 gm, 51 cm, who cried immediately. Only the forehead showed light forceps marks. These disappeared within a few days. Considering the highly situated head and the less favourable position of the forceps the delivery was unexpectedly easy and quick. The placentae were expelled twenty minutes later. There were no complications beyond slight atony and bleeding for the first half hour:

As prophylaxis a vitamin K injection was given to the baby, and penicillin for the first three days to the mother. Post-partum period was uneventful for both mother and child.

SUMMARY

Mention of etiology, symptoms and prognosis in constriction ring dystocia.

Improved prognosis due to a combined treatment of antispasmodics and active intervention. Delivery under protection of amyl nitrite inhalation in cases of constriction ring dystocia was introduced by *Gilliat*.

Amyl nitrite treatment simple, inexpensive, practically without danger, and highly effective.

Reference is made to cases of constriction ring dystocia to illustrate the above. Four case histories summarized, the fifth given in detail. This last was a typical case of a pronounced constriction ring (with twins), treated by amyl nitrite inhalation and high forceps delivery, which proved unexpectedly easy.

ZUSAMMENFASSUNG

Die Aetiologie, Klinik und Prognose beim Bandl-schen Ring werden erwähnt. Die verbesserte Prognose wird verursacht durch die Kombination von Behandlung mit Spasmolytica und Entbindungsoperation. Entbindung unter dem Schutze der Amylnitritbehandlung beim Bandl-schen Ring wurde eingeführt von Gilliat. Die Amylnitritbehandlung ist einfach, billig, so gut wie ungefährlich und überaus effektiv.

Fünf Fälle von Bandl' Ring zur Beleuchtung der erwähnten Verhältnisse werden referiert. Die vier Krankenberichte werden summarisch referiert, der fünfte mehr eingehend. Dieser war ein typischer Fall von ausgesprochenem Bandl-schen Ring bei einer Zwillingsgeburt, behandelt mit Amylnitritinhalation und Entbindung durch hohe Zange mit unerwartet leichtem Verlauf.

RÉSUMÉ

Étiologie, symptomatologie et pronostic de dystocie par l'anneau de Bandl sont mentionnés.

L'amélioration actuelle du pronostic est due à la combinaison de traitement par remèdes spasmolytiques combiné avec délivrance opératoire.

Dans des cas de constriction de l'anneau de Bandl c'est Gilliat qui le premier s'est servi d'amylnitrite en procédant à la délivrance opératoire.

Le traitement d'amylnitrite est simple, peu coûteux, presque sans risque et très efficace.

Suit la description de 5 cas de dystocie par l'anneau de Bandl. Les 4 journaux d'observation sont rapportés sommairement, le 5^{ième} de manière détaillée. Ce dernier cas présente une évidente dystocie par l'anneau de Bandl lors d'un accouchement gémellaire, traitée par inhalation d'amylnitrite et par délivrance à forceps. haut extrêmement facile.

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D. Prytz, Amtssygehuset, Haderslev.

Contribution to the Surgical and Chemotherapeutic Treatment of Brain Abscesses

*A Report of 77 Cases with Special Reference to Otogenic
and Rhinogenic Abscesses.*

By

MOGENS ROTWITT SCHMIDT

A brain abscess is one of the most serious complications met with. Its treatment is mainly surgical. The earliest procedure was insertion of a drain into the abscess cavity, but the patients usually succumbed to meningitis and progressing encephalitis. *Lemaitre's* method, introduced in 1919, was therefore a big step forward as it excluded the subarachnoid space. After puncturing the abscess with a brain needle he inserts a probe through the opening. Along this probe he slides a filiform rubber tube of a larger calibre. Acting like a foreign body the latter stimulates the formation of connective tissue in the subarachnoid space, and this reduces the risk of pus seeping in. During the subsequent days the drain is substituted by others of an ever wider diameter, until the tube has a lumen large enough to permit drainage of the abscess. When a capsule has formed around the abscess it may be removed. *Dandy* tapped the abscess several times before removal. Unlike these "closed" methods we have the *Feuchtinger-Leidler* technique, employing dilatation of the puncture opening and filling of the abscess cavity with iodoform gauze which is left for some weeks, and *King's* "marsupialization"

(1936 and 1937) with wide removal of the brain tissues covering the abscess. The cavity is filled with iodoform gauze in the form of a Mikulicz drain which can be removed gradually as the bed of the abscess approaches the surface. The edges of the abscess may be sutured to the galea (*Horrax* 1938). The last-mentioned methods are used in cases of large abscesses close to the surface. They result in a rather large cortical lesion and scar, but seldom in recurrence. An entirely different technique is the one advocated by *Clovis Vincent* (1938) in which the abscess is removed like a tumour. The abscess must be surrounded by a well-defined capsule, and the operation cannot be performed in the presence of major encephalitis in the surrounding brain tissue and not through infected areas.

The period elapsing until a capsule has formed around the abscess is critical, not only because of the increasing intracranial pressure, but also due to the progressing encephalitis which may result in perforation to the cerebrospinal fluid system and fulminant meningitis. The same danger is lurking after the operation. Chemotherapy has afforded a great help during this critical period.

In evaluating the results of the treatment of brain abscesses, a distinction must be made between 3 epochs: the time before the advent of chemotherapy, the era of the sulpha drugs, and the time after the advent of penicillin.

As regards the first epoch, the results improved perceptibly as progress was made in diagnostic methods and operative technique (especially after the introduction of *Lemaitre's* method). Up to 1920 the mortality was about 90 per cent, but from that time until the advent of sulpha drugs it was 60-70 per cent. In Denmark the subject has been elucidated by *Borries*, *Juul*, *Lund*, *Mygind*, *H.*, *Mygind*, *S. H.*, *Thornval* and *Vammen*. The sulpha drugs brought the aggregate mortality down to about 50 per cent. (*Peuch*), but it is difficult to decide to what extent these improved results were due to the *Clovis Vincent* technique which was introduced about the same time as the sulpha drugs.

It is, however, penicillin which has marked the most striking advance in the prognosis of brain abscesses. *Peuch* found a mortality of 16 per cent. among a series of 13 cases in which surgery was supplemented with local and universal penicillin. Seven of these cases were oto-rhinogenic and 6 were cured. *Le Beau*, in 1946, reported 14 cases of brain abscess cured by complete extirpation in one stage and penicillin, whereas 3 patients were lost after the same operation before penicillin was available. *Riskær* has collected the results obtained in the treatment of oto-rhinogenic brain abscesses receiving penicillin in Scandinavia from 1945-47 (read before the Danish Otological Society in May 1949). The series comprises 14 patients of whom 7 died. In 5 instances the condition was not diagnosed until the post-mortem examination. Of the 9 operated cases 2 died. Both patients were very ill before the operation.

WRITER'S SERIES

The series comprises a total of 77 cases of brain abscess treated at the University Hospital, Copenhagen, Department of Neurosurgery, from 1935-1948. Twenty-one were otogenic or rhinogenic, 56 of a different ætiology. In Table 1 all the cases are grouped by ætiology. It is difficult to set out the localization in tabular form, because of the numerous cases of multiple abscesses and the common localization on the border between the various lobes.

It is apparent from the table that the oto-rhinogenic abscesses make up the largest group (21). Next in size is the group in which the brain abscesses were due to infection of the lungs and pleurae (19). Then follows an almost equally large group of unknown ætiology (17). Several of these patients reported a history of minor cranial traumas which, however, had either occurred too long before the presumed onset of brain abscess or been too mild to be attributed with any importance. Cranial

TABLE 1.

The brain abscesses grouped by ætiology.

	Arising from	Number	Solitary	Multiple	Total
Oto-rhinogenic brain abscesses	Acute otitis	5	3	2	
	Chronic otitis	8	5	3	
	Frontal sinusitis	6	3	3	21
	Ethmoidal "	1	1	0	
	Sphenoidal "	1	0	1	
Brain abscesses of other ætiology	Seq. of pneumococcal meningitis	1	1	0	
	Seq. of ventriculography	2	2	0	
	Infection in lungs and pleurae ..	19	2	17	
	Infection in subcutaneous tissue	3	0	3	
	Infection in bones	4	4	0	56
	Infection in joints	1	1	0	
	Cranial injuries	9	8	1	
	Unknown ætiology	17	13	4	
Total		77	43	34	77

injuries were found to be fourth in order of frequency as an ætiological cause in this series (9).

Infection in the middle ear and accessory nasal sinuses is, however, an even more common cause of brain abscess than these figures lead one to believe, as they are in several instances treated by oto-rhinologists and never admitted to neurosurgical departments.

It is, moreover, apparent from the table that the otogenic and rhinogenic brain abscesses were solitary in 12 cases and multiple in 9, whereas the corresponding figures applying to the abscesses of other ætiology are 31 and 25 respectively. In other words, the ratio solitary to multiple cases of oto-rhinogenic brain abscess is practically the same as in the cases of some other ætiology,—only the group of abscesses originating in intrathoracic infections showing a sure prevalence of multiplicity. Beforehand, one would also expect comparatively fewer cases of multiple abscesses in the oto-rhinogenic group than in the others which must predominantly be of metastatic origin.

The localization of the 21 oto-rhinogenic cases was as follows: 7 in the frontal lobes, 11 in the temporal lobes, 1 in the cerebellum, and 2 cases of multiple abscesses localized in the cerebellum as well as in the cerebrum.

Treatment.

As chemotherapy has proved of such immense importance to the results, the main groups will be divided accordingly. No distinction will be made between brain abscesses above and below the tentorium, because of the very few cases with the abscess in the cerebellum. The latter occurred in only 4 cases 1 of whom was cured and 3 died. Of them 2 were moribund when admitted and died on the same day in spite of operation and penicillin. The 3rd patient died 6 weeks later presenting symptoms of bulbar paralysis.

TABLE 2.

Results of treatment with and without chemotherapeutic agents.

			Operated cases			
			Total	Number	Cured	Dead
Otogenic brain abscesses	Acute	Pre-sulpha	3	3	1	2
		Sulpha	1	0	0	0
		Penicillin + sulpha	1	0	0	0
	Chronic	Pre-sulpha	0	0	0	0
		Sulpha	4	4	3	1
		Penicillin + sulpha	4	4	3	1
Rhinogenic brain abscesses	Pre-sulpha	0	0	0	0	
	Sulpha	6	5	4	1	
	Penicillin + sulpha	2	2	2	0	
Brain abscesses of other ætiology	Pre-sulpha	11	5	1	4	
	Sulpha	32	27	9	18	
	Penicillin + sulpha	13	11	6	5	

It will be seen from Table 2 that among the *oto-rhinogenic* cases 3 were operated *without* receiving chemotherapeutic agents. Two of them died. Eleven received sulphonamide, but two did not

undergo operation. One of these died 24 hours after hospitalization. The patient was found to be suffering from multiple abscesses arising from a pus-filled sphenoidal sinus. The remaining 9 cases underwent operation and of them 2 died. The first fatal case was one of cerebellar abscess following chronic otitis, who did not succumb until 6 weeks after the operation. The cause of death is unknown. The second patient who could not be saved had an abscess of the frontal lobe following frontal sinusitis. He had previously been submitted to resection of the frontal sinus including division of the dura due to a subdural abscess. The brain had been punctured. After that a brain abscess developed and the patient died from purulent meningitis 12 days after the operation for the brain abscess.

In addition to the operation, penicillin and sulphonamides were administered to 6 patients of whom all were cured but one who had had a radical operation for a cholesteatomatous otitis a fortnight prior to admission. Purulent meningitis was diagnosed, 2000 cells per c.mm. Four ill-defined abscesses were removed from the temporal lobe, and the patient died exhibiting pneumonic symptoms 4 days later.

As to the group including *brain abscesses of other ætiology*, Table 2 shows that among the 11 patients who did *not* receive chemotherapy, 6 were not operated upon, as they were either moribund, dying a few hours after admission (3) or were inoperable due to the localization of multiple abscesses (3). Among the 5 patients who underwent operation 4 died, 3 of them from meningitis, and the 4th not until 2½ months later from unknown cause at another hospital.

The group treated with sulphonamide, but not with penicillin, counts 32 patients. In 5 non-operated cases the diagnosis was not made until post mortem. The patients were found to have been suffering from multiple small abscesses which had escaped detection by ventriculography and in several cases diagnostic trephining. Of the 27 operated cases 9 were cured and 18 died. Of the latter 5 had thoracogenic brain abscesses, multiple in 4

and a solitary, frontal abscess in 1 who exhibited symptoms of severe basilar meningitis. In 6 of the 18 fatal cases the ætiology was unknown, in the remaining 7 it was infection in bones, joints, subcutaneous tissue, and complicated fractures of the skull.

The last group received penicillin as well as sulphonamide. Two were not submitted to operation as one was moribund upon admission and died without operation because of perforation of an abscess of the occipital lobe to the ventricular system, and the other was inoperable due to multiple abscesses in the cerebrum and pons. Among the 11 operated cases 6 were cured and 5 died. Among the fatal cases 4 were suffering from thoracogenic, multiple brain abscesses and 1 from a cerebellar abscess following a fracture of the skull.

TECHNIQUE

Surgery:

D i a g n o s t i c: Ventriculography was done in practically all cases, supplemented in 7 with cerebral angiography or suboccipital encephalography. In 12 cases these examinations gave doubtful results, e.g. in cases with multiple small abscesses. Encephalography failed in only one case of a large solitary abscess.

T h e r a p e u t i c: All the patients were operated upon by one of the following procedures:

- (1) Insertion of a drain after the abscess had been located by puncture through a burr hole.
- (2) Marsupialization and insertion of a Mikulicz drain.
- (3) Evacuation of the abscess by suction and extirpation of the capsule.
- (4) Complete extirpation of the abscess in one stage.

The procedure chosen in each individual case depended on the size and site of the abscess and the patient's general condition. The method of complete extirpation without opening the abscess was used wherever possible.

Chemotherapy:

The sulphonamide preparations used were Lucosil, Alfamol, M & B 693, Streptamid, and sulphathiazole. The doses were those used in pneumonia, i.e. 1 g. 6-8 times daily, either by mouth or intramuscularly. Often the walls of the operation cavity were powdered with the drug. Penicillin was given in the form of intramuscular injections, as a rule 10,000-20,000 units every 3 hours, in cases of severe meningitis supplemented with injections into the cisterna magna of 5000-15,000 units once or twice daily. When drains were inserted into the abscess cavity it was washed with a penicillin solution containing 1000-2000 units per cc. through the drain twice daily.

DISCUSSION

It is evident from the literature as well as from the writer's series that chemotherapy meant an immense advance in the treatment of brain abscesses and that penicillin has been of the greatest prognostic significance. Neither diagnostic nor surgical methods have changed much during the period while sulphonamide was the only chemotherapeutic agent and the period while sulphonamides could be supplemented with penicillin. The results of treatment during these two periods are, therefore, directly comparable, as the severity of the cases appears to have been the same. As patients with brain abscesses will certainly die, if not operated upon, only the operated cases in both groups are included. In spite of the small number of oto-rhinogenic brain abscesses involved, the writer feels justified in expressing the results in per cent. for the sake of perspicuity. The results of the different surgical procedures, on the other hand, are not stated, as the comparable groups would become too small when regard is also paid to ætiology and chemotherapy. It is, however, our impression that when using penicillin one may choose a more radical procedure than otherwise.

TABLE 3.

The significance of penicillin in the treatment of oto-rhinogenic brain abscesses and brain abscesses of other ætiology.

	Number of operated cases treated with chemotherapeutic agents	Number treated with sulphonamides		Number treated with penicillin + sulphonamides	
		operated	died	operated	died
Oto-rhinogenic brain abscesses . .	15	9	2 (22 %)	6	1 (17 %)
Brain abscesses of other ætiology	38	27	18 (66 %)	11	5 (45 %)
Entire material	53	36	20 (56 %)	17	6 (35 %)

It is apparent from Table 3 that the mortality from oto-rhinogenic brain abscesses was 22 per cent. with sulphonamide as the only chemotherapeutic agent, and 17 per cent. when this was supplemented with penicillin. The corresponding figures applying to brain abscesses of other ætiology were 66 and 45 per cent. Among the whole series the mortality has fallen from 56 to 35 per cent., roughly speaking the same fall in all 3 groups, if allowance is made for the few cases in the first group.

The much better prognosis of oto-rhinogenic brain abscesses than of those of other ætiology is in part due to the fact that a great part of the latter group is made up of metastatic abscesses which are often multiple and of a deeper situation.

The greatest advantage of penicillin is that it affords better control of pre- and post-operative meningitis and encephalitis than sulphonamides alone. One is therefore in a position to await the most favourable time for operation, i.e. when the abscess is well-defined. A brain abscess should be treated like meningitis originating in a known focus, i.e. with penicillin, sulphonamide, and operation. In the cases of severe meningitis intramuscular penicillin was supplemented with suboccipital administration. This procedure did not cause untoward effects worth mentioning. Compared with the serious nature of a brain abscess the pleocy-

tosis which often attends intrathecal administration of penicillin is negligible.

In our series positive bacterial findings were reported in pus from the abscess in 28 cases: staphylococci in 12, streptococci in 8, pneumococci in 6, proteus in 1, and *alcaligenes* in 1. In 12 instances no bacteria were demonstrable in the pus. In addition to determining the genus of the bacteria, it is necessary also to determine the resistance of the bacteria present in the abscess and the spinal fluid. An excellent method for this purpose has been advocated by *K. A. Jensen*. It is only by utilizing all the diagnostic, surgical, and chemotherapeutic means available, that one can hope to obtain the best result in the treatment of a brain abscess.

SUMMARY

The author briefly reviews the various surgical methods in the treatment of brain abscesses as well as the results of treatment, reporting, at the same time, a series of 77 cases, 21 of which are oto-rhinogenic. The ratio solitary to multiple cases of oto-rhinogenic abscesses is practically the same as in the cases of some other ætiology, metastatic abscesses from intrathoracic infections being excepted; in the latter group there is a clear predominance of multiple abscesses. The results of the surgically treated cases of both groups are set out according to the chemotherapy employed. As regards the entire material of operated brain abscesses in this series the mortality has decreased from 56 to 35 per cent. by supplementing sulphonamides with penicillin. In the otorhinogenic cases the corresponding figures are 22 and 17 per cent., and in the cases of other ætiology, 66 and 45 per cent. The method of complete extirpation is used wherever possible. Penicillin was given intramuscularly and in cases of severe meningitis also in the form of injections into the cisterna magna and local applications. Finally, the author emphasizes the significance of determining the genus and resistance of the bacteria.

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Cephaloceles Posterior Orbitae

A General Survey with Report of a Case

By

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By cephalocele posterior of the orbit is understood cerebral hernia, emanating from the fossa cranii media, penetrating into the posterior part of the orbit behind the bulbus oculi, through a preformed or non-preformed opening in the orbit wall.

Cephalocele posterior of the orbit belongs to the group of basal cephaloceles. Besides these, by far the rarest of occurrence, there are occipital, frontal, parietal, and lateral cephaloceles. Cephalocele of the anterior orbit, generally emanating from the nasofrontal, belongs to the frontal cephaloceles and is much more frequently observed than the posterior affections. *Stadfeldt*, who was the first in this country to compute the available material, found in the literature on the subject, up to 1902, twenty anterior and eight posterior cephaloceles. It has been the subject of some discussion whether a certain case of the latter group should be counted as belonging to that group, or reckoned among the anterior cephaloceles (*Oettinger's* case). *Max Schmidt*, who in 1927 reported a case, besides surveying available reports, did not include it among the posterior cephaloceles. Nor is this the case in the present report, because—as first stated by *Peters*—it appears from the description that the deficiency of the orbit wall was located so anteriorly that it is reasonable to suppose that

it originated from the nasofrontal, and not, as held by *Stadfeldt*, from the fossa cranii media.

Realì collected 141 cases of cephalocele, thus distributed: occipital 86; frontal 33; parietal 12; lateral 8; and from the basis cranii 1. Computations made by *Houel*, *Lawrence*, *Wallmann*, and *Larger & Lindfors* are in agreement with *Realì's* distribution of favourite sites, whereas *Deloff* finds the number of frontal cephaloceles to exceed the number of occipital.

Some dispute has arisen as to the term *cephalocele*, as the hernial content has not always consisted of cerebral tissue in affections with characteristic symptoms, and in cases where bone deformities, ascertained through post-mortem or X-ray examination, were of the nature of hernial openings. Other designations have, therefore, been suggested and applied for short periods, aiming at a specification of the hernial content—meningocele, encephalocele, meningocephalocele, hydroencephalomeningocele, and encephalocystomeningocele. The last mentioned designation was proposed by *Muscatello*, who was of the opinion that the affection was caused by cystic arachnitis, a view he supported, inter alia, on the findings of microscopic changes in extirpated tissue of the cephalocele (epithelial) proliferation, cystic degeneration, and invasion of the vessels).

In the following survey, comprising thirty-one cases of cephalocele of the posterior orbit, only such cases have been included in which the symptomatology is characteristic and where X-ray or post-mortem examinations of the cranii have established the presence of a hernial formation, with contents originating from the fossa cranii media, into the orbit behind the bulbus, either through a defect of the orbit wall or through an enlarged preformed opening, besides cases in which explorative operations of the orbit have revealed "tumors" consisting of brain tissue—with or without membranes (whether cystically degenerated or not)—and cerebrospinal fluid.

A comparison of the comparatively high number of congenital cephaloceles and the frequency of unilateral bone deformities

in the form of failing ossification with the fact that in a single case only there have been meningeal symptoms before the diagnosis of cephalocele symptoms, in my opinion shows that it is more natural to consider the cystically degenerative changes in the arachnoidea (a) as secondary in relation to the actual defect through which the hernial formation penetrates, and (b) as a natural consequence of the altered pressure and gradual compression which corresponds to the hernial opening—in a manner exactly similar to that which can be seen during operations on incipient incarcerated hernia. Nor does the fact that the post-mortem examination of seven out of eight patients, who died after operation, revealed degenerative inflammatory changes of the meninges, support the view that this is the fundamental, primary affection. On the contrary, going through the reports, it appears that in all these seven cases the meningeal symptoms appeared post operationem, presumably as a consequence of exogenic infection (the cases concerned being from a group of fourteen who underwent operations: five incisions, seven excisions, and two punctures).

The *preformed* openings through which cephalocele of the posterior orbit may penetrate are the optic foramen, the sphenoid and sphenomaxillary fissures, and the posterior ethmoidal foramina. They may be either of normal size or enlarged. Generally, enlargements are unilateral, and may affect all openings or one of them only.

The *non-preformed* openings may be *congenital deficiencies* (incomplete ossification, generally unilateral, or birth traumata), *traumatic defects of later origin*, or *defects caused by other previous or simultaneous disease*. (Listed in order of frequency they are: bone erosion due to aneurysms, malignant tumors, inflammatory processes, angiomas, von Recklinghausen's disease, Paget's disease, and internal hydrocephalus).

The soft meninges and brain tissue as a rule form component parts of the hernial formation, whereas the dura mater generally is not involved in the later stages of the affection, but bursting

early in the affection's development, together with the bone edges, forms part of the hernial opening. Only in such earlier stages as are not generally well developed, although marked by symptoms characteristic of cephalocele of the posterior orbit, the dura mater is found to form part of the hernial sac.

As a further sign that the primary affection, in the great majority of cases, is an abnormal development in early fetal life the apparent existence of a gradual transition may be emphasized. It would appear likely that this transition starts as exemplified in *Borochovic's* cases (1930) (one of which had double anophthalmos with orbital cyst (Number four of four siblings, a girl aged seven), and her sister (Number three of four) had dextral anophthalmos and sinistral microphthalmia, both cases with pronounced congenital defects of roof as well as of posterior wall of the orbit). The transition might pass through the case described by *Tauber* in 1900 (with unilateral microphthalmia and failing ossification of posterior wall, roof and bottom of the orbit, whereby the cranial cavity, the orbit, and the maxillary sinus of the affected side form one single cavity), to the case reported by *Cohen* in 1927 with microphthalmia and enlarged optic foramen on the same side; and it might further be emphasized that the microphthalmia which appears in four of the thirty-one cases collected here must rather be considered examples of abnormal development—like the cranial malformations—than a secondary change as a consequence of the increased pressure in the orbit.

Further, the disease is characterized by being, in most instances, a congenital affection which may become manifest or aggravated as the result of traumas or the presence of some other disease. The affection progresses slowly. In individual cases only does it manifest itself by serious symptoms, and but rarely by general cerebral symptoms—such symptoms, when present, being epileptic fits, defective speech and memory.

The material on which the present survey is based comprises in all thirty-six cases, reported as cephalocele of posterior orbit. From these must be deducted five cases: one case, reported by

Oettinger in the *Klin. Monatsbl. f. Aughlk.* 1874, where the possibility cannot with certainty be excluded that the cephalocele emanates from the fossa cranii anterior, as, besides a deficiency corresponding to the ethmoidal bone, the orbital plane is to all intents and purposes absent. Second, the present report does not include a report by *Schousboe* in the *Bull. de la Soc. d'ophtalmol. de Paris*, 1927, and one by *Kalt* in the same bulletin of 1930, besides a case reported by *Tietze* before a German meeting of ophthalmologists in Munich, 1935. In respect of the three latter cases it may be said that the information available is too scanty to allow with certainty their inclusion in the group of cephaloceles of the posterior orbit. Finally, *Bonnet* reported a case in 1937, but in the same year *Aranowich* protested against its classification as the affection in question, since it was a clear case of hernia of the dura mater. The remaining thirty-one cases have been collected from available literature, published between 1841 and 1948. Cases concern fifteen females and nine males; in respect of seven patients there is no information as to sex. The ages of the patients at the first examination are between thirteen weeks and seventy-seven years. By far the greater majority consists of young persons: twenty-two patients are under thirty, and three over thirty, while there is no statement as to age in respect of six patients. In twenty-one cases where the patients have been especially interrogated there were no familial dispositions to eye diseases or congenital malformations. In twenty cases the affection has been accompanied by symptoms from shortly after birth, though to a comparatively small degree. In two instances there have been serious traumata (*Lücke* and *Tauber*): one being a case where a blow on the right eye quickly developed pulsating exophthalmos; the other a case of head trauma at the age of fifteen, with consequent blindness—this latter case has presented progressive symptoms of cephalocele of posterior orbit since birth, whereas in the former case the patient was always healthy up to the accident, and free of previous eye affections. In thirteen out of thirty-one cases tumors

have at the initial examinations been felt in the orbit, most frequently located medially to and passing in behind the bulbus oculi. The consistency of the tumors was in all cases: soft, yielding, and slightly elastic.

In twenty cases the bulbus was displaced in relation to its original position in the orbit: in eighteen cases downwards and laterally, and in only two cases downwards and medially (*Wheeler* and *Jaensch*). In *Jaensch's* case there was, besides the anomalous posterior wall of the orbit, a defect in the lateral wall through which the cephalocele made its way.

In fifteen cases the mobility of the bulbus was limited.

In twenty-eight cases there was unilateral exophthalmos, fairly equally distributed among right and left eyes. In twenty-six of these patients exophthalmos was pulsating with greater or smaller oscillations, in all cases synchronous with the carotid pulse.

In thirteen of the patients it was possible to rectify the protrusion of the bulbus by a slight pressure on the bulbus, resulting in a simultaneous further protrusion of other contents of the orbit, but without causing cerebral symptoms. In three cases attempts at reposition caused vertigo or nausea (*Gala*, *Lunding Schmidt & Jensen*, *Strandberg*). In no case did changes in the pulsation of the bulbus appear with the variation of the position of the head when in an upright position, while *Jaensch* (1941) in one case reported considerably reduced bulbar pulsation after a prolonged period of quiet rest on the back.

Kulbi mentions aggravated pulsating exophthalmos at coughing, sneezing, and forced contraction of the abdominal muscles, observations that correspond well with those of *Gala's* to the effect that protrusion decreases in proportion to the quantity of cerebrospinal fluid withdrawn by lumbar puncture, and that the cerebrospinal pressure increases when reposition of the protruding bulbus is attempted.

Wheeler observed that the pulsation of the eyeball disappeared, and the protrusion diminished, under avertin anesthesia.

Sixteen patients had palpebral edema: thirteen of the palpebra superior, and three of the palpebra inferior. Eight had ptosis.

The size of the eyeballs in eighteen cases is stated to have been natural, whereas there were four cases of microphthalmia (*Taube, Delpech, Parson, and Cohen*).

Furthermore, in *Cohen's* case reduced tension and horizontal nystagmus are reported.

The affected eyes in seven patients had vision reduced from $\frac{6}{12}$ to total blindness.

Three patients presented diplopia (*Dandy, Jaensch and Wheeler*), and on examination two cases of changed visual fields were revealed (*Dandy*: slight concentric contraction; *Jaensch*: annular scotoma).

Ophthalmoscopy revealed changes in five cases. In three patients (*Jaensch, Dandy, and Stadfeldt*) there was overfilling and tortuosity of veins. One patient (*Lagleyse*) had blurred papillary edges, and in one case (*Parson*) there was coloboma of the optic nerve.

In three cases only was it possible to decrease the pulsation of the bulbus by compressing the carotid.

Of other eye symptoms one of *Jaensch's* patients presented interstitial keratitis; the one of *Cohen's* had iris atrophy, cataract, and stiff pupil, and *Stadfeldt's* patient had coloboma of the iris.

In two cases there was audible vascular bruit, in the one objectively ascertained, in the other subjectively felt.

Cranial changes were many and characteristic: twenty-one patients had enlarged orbit on the affected side. Twelve had visible asymmetry of cranium, and in nine of these the temporal region was notable prominent. Four of these same nine patients, besides cephaloceles of the posterior orbit, had cephalocoele of the temporal region (*Jaensch* (1926 and 1941), *Schreyer & Sprenger*, and *Strandberg*). Two of these deserve further mention. The case published by *Jaensch* in 1926 had, moreover, incipient cephalocoele auricularis, the investigation at the ear clinic revealing a tense, pulsating prolapse of the dura mater in the external

auditory canal. *Schreyer & Sprenger's* patient also had cephalocele auricularis, but with the peculiarity in respect of the cephalocele in the temporal region that the hernial opening was not—as usually seen—formed by suture edges or by deficiencies corresponding to a suture, but by the temporal squama directly, in the middle of which the affection was located.

In seven cases there was enlarged optic foramen, and in six cases enlargement of the sphenoid fissure, whereas the posterior ethmoidal foramen was enlarged and formed the hernial opening in only one case (*Zitowski*).

In twelve cases there was palpable deficiencies in the orbit wall.

X-ray or post-mortem examinations in fifteen cases revealed deficiencies in the orbit wall. Eight were located in the posterior wall, four in the hindmost part of the roof, and three in the side walls, (two medially and one laterally) (*Jaensch*). In two cases the sella turcica was enlarged.

Other cranial defects causing cephalocele of the posterior orbit were the absence, in five cases, of the lesser wing and/or parts of the greater wing of the sphenoid (*Jaensch* (1928 and 1941), *Ecklentz*, *Scullica*, and *Strandberg*).

In two patients there appeared, simultaneously, cephalocele from the fossa cranii posterior. In both cases the defect was located corresponding to the occiput (*Jaensch* and *J. van der Hoewe*).

In respect of six patients there are reported fistulae from the ventricular system to the cephalocele.

The most serious defect has been described in *Tauber's* case with imperfect ossification of the lesser wing of the sphenoid, of the base of the greater wing of the sphenoid, of the cribriform plate of the ethmoid, and of the upper and lower orbit wall.

Arranged according to frequency of appearance the eye symptoms of cephalocele of the posterior orbit then are as follows: a slowly developing unilateral pulsating exophthalmos, appearing mainly in younger persons, in the majority of cases synchronous

with the pulse, and redressable by pressure on the bulbus, in most cases without accompanying cerebral symptoms, but sometimes with vertigo and nausea. Exophthalmos may change proportionally with the cerebrospinal pressure, whereas the pulsation in the majority of cases remains unaffected by compression of the carotid artery of the affected side. The eyeball is displaced, most frequently downwards and laterally, and in few cases downwards and medially if the deficiency is located in the lateral wall of the orbit. There is hampered movement of the bulbus, dependent on the size of the encephalocele. There is a palpable, soft, elastic tumor in the orbit. There is edema of palpebrae, most frequently of the upper and in some cases of the lower palpebra. Ptosis, reduced vision, and microphthalmia must in all probability be regarded as defective development in the same manner as the skeletal deficiencies found, rather than secondary phenomena; further there might be diplopia, central changes in the form of venous congestion, incipient papilledema, and coloboma of optic nerve, when the hernial opening of the cephalocele is formed by an enlarged optic foramen. In single cases there is changed visual field, bruit, reduced tension (observed only in cases with simultaneous microphthalmia), and nystagmus.

Operative treatment has been reported in twenty-three cases.

In three cases ligation of the carotid artery on the affected side has been made; no improvement.

In five cases incision of the palpated orbital tumor has been carried out.

In seven cases excision in part of the hernial formation was performed (in one of the cases without ligation of the hernial sac).

Two cases have been punctured.

Within the groups subjected to incision, excision, and puncture, fourteen cases in all, eight are reported to have died following operation. In seven cases the cause was postoperative meningitis, in one case "cerebral crisis".

In four cases transplantation has been carried out with living tissue.

There is one case of trepanation with dural substitute, and one of craniotomy with Gel-film plastic.

In the six last-mentioned cases consequences were not fatal, and in all cases the symptoms were noticed to diminish; the bone healed well in the four cases of transplantation.

Although the number of operations carried out is low, and the descriptions in several cases incomplete, the results seem to indicate that the patients are best served by operations in the manner of hernial affections, i.e. craniotomy, reposition of the contents of the hernia, substitution according to defect—bone transplantation in smaller defects, and in more comprehensive cases substitution by Gel-film of suitable thickness to the circumference of the defect, and, dural substitute if and when practicable.

In conclusion a report will be given here of a case of cephalocele of the posterior orbit from the University Hospital, Copenhagen.

The patient is a girl, aged 6, in whom pulsating exophthalmos had been diagnosed, and whose case was referred to the Eye Department of that hospital on 23 February, 1948.

She has had the usual childhood's diseases, without complications. No familial dispositions for eye affections or congenital malformations. She is number four of four siblings. Previously always in good health. Mental and physical development natural, corresponding to age.

The present affection has been observed by her mother during the last year, manifesting itself by pulsation of the right eye in the orbit, synchronous with the pulse, besides by growing asymmetry of the cranium with thickening of right temporal region.

No other abnormalities observed by her mother.

At objective examination is found an apparently normal and healthy child. Physical and mental development corresponding to age. Stethoscopy of heart and lungs: natural.—Abdomen: soft, natural.—No neurological abnormalities.

Cranium: slight asymmetry of face. Watch-glass-shaped prominence of right temporal region as compared with left side. Corresponding to and along the sphenoparietal suture is felt a cranial defect, 3 to 5 mm. broad and just under 2 cm. long. No hernial formation is felt here, but when pressed a soft elastic resistance may be noticed, and it is only slightly tender.

Eye examination: vision both eyes: 3/4,5 without correction.

Right orbit is larger and more ovoid than left. No palpable deficiency of orbital wall. Slight protrusion of right eyeball, which is noticed to pulsate synchronously with the pulse, with varying oscillations, maximum 3 mm., minimum scarcely visible. Neither protrusion nor pulsation is altered by rotation of the head. During repeated attempts at compression of the carotid of the affected side, it appears in a single instance as if the pulsation of the eyeball is declining; it returns, however, before the compression is discontinued.

Exophthalmometry (ad modum Hertel): right side 15 mm. as against 13 mm. on left side. The protrusion may be redressed by pressure, thereby causing slight prolapse of content of upper orbit accompanied by a slight feeling of discomfort, slight nausea, and uncharacteristic vertigo.

No audible bruit at auscultation of cranium. No nystagmus or double vision. The bulbus can be moved freely in all directions, to the same extent as the left eye. Bulbus displaced slightly downwards and laterally. No strabismus.

Cornea, conjunctiva, anterior chamber, lens, and iris: natural.

Ophthalmoscopy reveals natural conditions on both sides. At X-ray examination of the cranium (Dr. Gilg), its shape and size are natural. The sella turcica is natural. Left orbit natural, while the right orbit is a little larger and more ovoid; corresponding to the whole background of the orbit is seen a large defect, the upper edge of which is clearly discernible, whereas it is difficult to locate its lower limit. The defect seems to affect very great proportions of the wings of the sphenoid. No signs of defects elsewhere in the cranium. The paranasal sinuses are weakly developed.

X-ray examination (Prof. Fl. Moeller) of the cranium is repeated after nine days, now showing: in the frontal plane, the right orbit is larger and more ovoid than the left. On the right side it is not possible to see the posterior wall, nor, on this side, any sphenoid fissure, and it appears as if the wings of the sphenoid are displaced upwards to a considerable degree, lying like an arc over the uppermost part of the orbit. The same phenomenon is noticed on a special exposure of the optic foramen, which in itself presents no abnormalities. Likewise, an x-ray photograph in the right lateral position reveals the same displacement, and one is inclined to conclude that pressure is being caused by an unknown factor which has dislocated it, and caused erosion of the posterior lateral wall of the orbit. No abnormalities of the paranasal sinuses can be demonstrated, but the frontal ethmoidal sinuses are very incompletely developed.

Planigraphy of the right orbit was then attempted, but the pictures are not so valuable as might have been the case, because the patient moved during exposures.

On 19 March 1948 she was moved to the Neurosurgical Department of the University Hospital for arteriography and possible operation. Here, eye examination and neurological examination gave results as above mentioned.

On 22 March carotid arteriography revealed a peculiar protuberance

of the carotid syphon on the right side, which may be forced, but the presence of partial carotid block is beyond doubt.

On 23 March 1948: ventriculography. Pressure: 140/100. Roentgenograms show no abnormalities.

Operation (Prof. E. Busch): Frontal skin incision over the anterior part of the right hemisphere. The tumor of the temporal region appeared to be but a blister formation in the bone over a strongly protruding temporal lobe. The sphenoidal wing was located extremely frontally, 2 cm. only from the orbital process, following the middle meningeal artery which was about 2 mm. thick. The fissure of Sylvius was very deep, whereas the bone itself, and especially the wing of the sphenoid, was thin as paper. It was removed laterally by forceps, whereupon the dura mater was opened. It was then possible to penetrate to the fossa media and to the posterior wall of the orbit where it appeared that no bone at all had formed; a thin incomplete membrane of connective tissue only parted the fossa media, corresponding to the temporal pole, from the orbital contents. There were no signs of tumor or aneurysm. The posterior wall of the orbit was covered with Gelfilm; whereupon complete suture of the dura mater. The wound was closed in the usual way. The patient stood the operation well. Postoperative course uncomplicated.

On 30 March 1948 the patient was sent back to the Eye Department, feeling completely well there. Faint pulsating exophthalmos still present, though to a considerably lesser degree. Dislocation of eyeball on the decrease. Patient discharged on 16 April, to report at intervals for continued control.

SUMMARY

From the literature between 1841 and 1948 have been collected thirty-one cases of cephaloceles posterior of the orbit, and a survey of the most prominent pathologico-anatomic changes is given. Various reasons are given in support of the view that this affection is a congenital malformation, caused by failing ossification, rather than a condition following cystically degenerative arachnitis—a view previously held. Directions for treatment are given, and in conclusion a recently diagnosed Danish case is reported.

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On Musicogenic Epilepsy

By

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Musicogenic epilepsy is a rare form of epilepsy in which the patient has a tendency to get epileptic attacks induced by music. This form of epilepsy really was first described in Russia, where in 1884 Merzjejevskij demonstrated a case in the psychiatric society of St. Petersburg.

For the following forty-five years very little was heard about m. ep., but in 1937 Mac Donald Critchley described eleven cases, of which he had a personal knowledge, and nine quoted from literature. In 1942 he mentioned further two cases and Taylor one. In 1947 David Shaw & Denis Hill gave an excellent survey and analysis of m. ep., based upon one instructive case of Jacksonian fits, induced by various kinds of music with a comprehensive discussion of the literature. EEG records from the left parieto-central region during a musicogenic fit were also given. They showed that a pure tone of 512 only affected the patient emotionally whilst within five minutes different kinds of music invariably induced a seizure. EEG demonstrated a cortical discharge of low voltage (30-40 μ volt) 6-7 c/sec. potentials synchronously and with equal amplitude from the two hemispheres. These abnormal waves began six to eight seconds after the apnoea initiating the fit.

This paper presents four cases and especially one case operated on by Dr. Busch.

A short survey of the clinical form of m. ep. shows that the

attacks induced by music may vary highly. In most cases the initial symptoms consist in a sudden slight blurring of the mind, a sensation of fainting or a complete stop of any psychic activity. Presently these symptoms are followed by a petit mal or grand mal with all their more or less alarming signs.

Critchley correctly warns against confounding with the more common acoustico-motor epilepsy induced by a sudden violent unexpected or long-lasting irritating and tedious noise.

In m. ep. the music acts as a trigger, releasing the patient's special form of epilepsy depending on the cerebral disease which is the basis of his epilepsy. In some cases of m. ep. the aura is rather long, enabling the patient to stop any further development of the attack by shutting off the radio, by running away from the dangerous music in a restaurant, etc. Unfortunately, however, the aura is generally too short to be of any aid to the patient, and in a second or less after he has been aware of the danger he is struck or bound by the evil spell of the music.

During the aura, if this is long enough, the patient is definitely changed emotionally; being either frightened, sad, anxious for the coming attack, or, on the contrary, and more seldom, he may have a feeling of brightness, an uncommon clearing up of the mind or even of a spiritual exaltation like the ecstasy experienced by Dostoiefsky.

The aura may further be accompanied by vegetative disturbances, such as pallor, mydriasis, salivation, etc.; but symptoms known from the uncinat attacks have not been described in m. ep.

The severity of the seizures may vary from the slightest petit mal to the most violent grand mal with or without focal initial or postparoxysmal symptoms.

Even the sort of music inducing the attacks may vary. Nearly every individual patient possesses his special sort or sorts of dangerous music. It seems as if the emotional factor in listening to music is of great importance. This even holds true when focal neurological signs can be found before, during, or after the attack.

Several patients seem to acquire their convulsions not only by hearing, but also by singing their ictogenic music or by mere discussion or remembrance of it.

When by facilitation this pathologically conditioned reflex is first developed, seizures may occur nearly instantaneously when the music starts but generally it does not set in till some seconds or minutes later. Hardly any patient gets his attacks every time he is exposed to his ictogenic music. Here as elsewhere in neuropathology the "trigger" only works when "the gun is loaded".

Several cases therefore have not been diagnosed because the patient was unable to demonstrate his seizures in the clinic, when the doctor played the assigned dangerous music for him.

As a rule m. ep. does not set in till the second or third decade. On the analogy of other forms of epilepsy, therefore, an organic disease of the brain, and here of the parieto-temporal lobe, must be the pathological base of m. ep.

No systematic survey has hitherto been given on the etiology of m. ep. No case seems to have been operated upon and no histological cerebral abnormalities have been demonstrated.

My supplement to the problems of m. ep. is based upon four cases, two of which have been given to me by courtesy of Dr. Eeg-Olofsson, Stockholm, but especially upon one case operated on by Dr. Busch.

CASE HISTORIES

Case I. Female born in Stockholm 1884 of a healthy family with no previous history, until in 1938, fifty-four years old, she developed epileptic petit mals and later even typical grand mals induced by classical music played on the gramophone.

Neurological examination in 1946 revealed nothing abnormal, but by EEG Dr. Frey found a general dysrhythmia of the low-voltage type with dominant intermingling of quick frequencies. No focal cortical abnormalities were to be seen, until music was played and provoked a range of slow 2-4 c/sec. waves from the right temporal lobe. During this the patient felt she "was going to have an attack," but no signs could be observed.

She was mentally deteriorated and had a bad memory. Under medical treatment she was kept free from convulsions.

Comment: Presumably the etiology in this case of m. ep. is a slight cerebral arteriosclerosis. On account of this and the good result of the medicamentation, neurosurgical treatment was declined.

Case II. Male born 1911 in Copenhagen. No epileptic disposition. Well educated bank clerk, left-handed, otherwise healthy.

Twenty-two years old he had a slight trauma of his right shoulder and right temple in a road accident. No immediate serious symptoms. Next day he suffered from headache and a little nausea, but for the next weeks he was quite well, until a month after his accident he fainted while listening to classical music.

This happened several times during the next two years. He was admitted to the psychiatric department of the Rigshospital in July 1935. Here no abnormalities could be found and no seizures induced by music or hyper-ventilation.

During the following ten years he was treated six times for short periods at "Filadelfia" in Dianalund, and here several seizures were induced by music. His attacks varied from a slight sensation of fainting to severe typical grand mals. Further, a few atypical paroxysms were seen. While he listened to music on the radio, he suddenly felt restless, his respiration stopped so that he was cyanotic, his gait was giddy, and as soon as he was brought to bed he fell asleep at once so deeply that he could not be awakened for several hours.

The type of music which was dangerous to him was classical lyric compositions. Songs or instrumental, string- or wind-instruments were equally noxious to him, whilst jazz and other modern music left him completely unmoved and unhurt.

Even discussion about music was able to elicit seizures, but only if the discussion affected his emotions.

Neurological examination revealed: body-type hypopituitary with overweight (weight nearly 16 stone (109 kg) and height 6 feet (182 cm)), but no focal cerebral signs. The encephalogram was normal. EEG showed general dysrhythmia more marked in the right temporo-parietal region where 5-7.5 c/sec. prevailed.

On account of headaches and mental reduction with emotional instability and irritability, he was sent to Dr. *Busch*, who by ventriculography found a dilatation of the right temporal horn.

At the operation in January 1939 Dr. *Busch* found a typical traumatic lesion of the right temporal pole. A dense fibrous plate in the cortex, the size of a penny, was excised, and a vein with predominantly arterial blood from the posterior part of the plate cauterized. Another sinusoid vein, however, directly communicating with veins from the Sylvian group, it was too risky to cauterize.

Microscopy of the extirpated prepate showed a typical traumatic affection

After the operation his state improved and he was free from seizures and quite all right for a whole year. But then again, in spite of antispasmodics, attacks returned with increasing strength and frequency as well as his headaches. His weight increased, too; and his memory was deteriorated. He attempted suicide by phenobarbital, but was saved.

Four years after his first operation therefore he was *reoperated* by Dr. Busch, who now loosened several vascular adhesions between the temporal cortex and the bone graft. A slight complete left-sided hemiplegia was seen the day after the operation, but otherwise no complaints. Again his state improved even though his mental abilities still were reduced, and his right-sided temporal headache persisted. Now and then he still had musicogenic attacks or faintings.

Three years after his second operation Dr. Busch found no focal neurological signs except by EEG, which showed a moderate dysrhythmia with slow potentials from both frontal lobes and the right parietal region, where phase reversals were ascertained.

Now, six years after his second operation, his condition is rather good. He has stopped taking antispasmodics and is able to fulfill his tasks in the bank rather satisfactorily; but twice or three times a year he still has his seizures when he happens to forget the danger of music.

Comment: This case of m. ep. of certain traumatic origin is the first one hitherto operated on. Two operations on the right temporal pole seem to have ameliorated the condition of this left-handed patient considerably, although he still may have musicogenic convulsions. A complete recovery could not be expected since a complete removal of the traumatic brain affection was too risky and might have given him a persisting hemiplegia and aphasia.

Case III. Female born 1913 in a healthy family. No reports of previous factors disposing her to her ordinary epilepsy with grand mals, which started in her twenty-eighth year.

For the first two years of her epilepsy she had about twelve seizures without any known releasing mechanism; but then she discovered that she got her attacks when she listened to music or if unexpectedly she either experienced joy or anxiety.

This condition lasted for four years. She was now admitted to the neurosurgical department of the Rigshospital. Here only a nystagmus to the right was found. X-ray of the skull revealed nothing abnormal but a very slight craniostasis and a slight frontal internal hyperostosis.

Encephalography showed a normal ventricular system, but EEG displayed a pronounced dysrhythmia especially from the right parietal lobe. By hyper-

ventilation some waves of high frequency from the left hemisphere were increased. While the prelude in A major by Chopin was played, focal phase reversals were observed from the upper part of the left precentral region; and a few minutes after the music had started, the patient got mydriasis and, upward turning of the eyes, and was unconscious with swallowing, snoring, and tonic spasms of the right arm and hand. The seizure ended in a state of general tonic extension for a minute, and was followed by a peculiar grasp-posture of the right hand and a tendency to upward turning of the eye-balls.

The patient was transferred to "Filadelfia" for medical treatment, but stayed here only for thirteen days. Two petit mals were observed without any connection with music, but she complained of irritability during morning- and evening-song in the ward, even if the door to her single room was closed all the while.

Comment: This case of cryptogenetic epilepsy shows that a musicogenic mechanism may arise later on and as a new pathophysiological feature in the cerebral disturbances which gives epileptic seizures.

Presumably, the left precentral region in this case is the primary epileptogenic area, but neurosurgical treatment was found too risky in proportion to her symptoms. At present, therefore, a final evaluation of her problems is impossible.

Case IV. Male born 1895 of a healthy and very intelligent Swedish family. He was carefully educated, happily married, and well established as a manager of a well consolidated firm. All fates seemed to cooperate to his benefit. But five years after his wedding his wife grew insane with a paranoid jealousy of her husband. She left him and went with their three children to her parents' home. Two years later she was admitted to an asylum, where she remained as a chronic insane. The children stayed with their grandparents, because, as a business man, he was unable to supervise their daily life.

In his loneliness he tried to forget his misfortune by listening to music, which he had never enjoyed before. He bought a gramophone and records with all the symphonies of Beethoven. Listening intensely every night to the music, he forgot his sorrow and in a few months he learned all the symphonies by heart.

Now in his leisure hours, on journeys, etc., he discovered that even the memory of the symphonies could check his bad spirits. Rather often he successfully applied this method of psychocatharsis.

A few months later he realised that while listening to classical music and especially to the Beethoven symphonies his mind became blurred, and that at the same time he for some seconds had a pronounced sensation of pleasure. In the following months this marvellous feeling now and then appeared

spontaneously and two years later, in 1932, he got this feeling once more, but now it came during a concert as an aura of a typical epileptic seizure induced by the music.

As this unfortunate event had occurred several times, it was now impossible for him to go to a concert, into a cinema or in a restaurant where he might be surprised by classical music. Even if he tried to fight against the imminent danger his attention was irresistibly fixed by the sonorous figures eliciting his nearly ecstatic feeling of joy; but a second or two later he fell down, losing consciousness and presently had general clonic spasms; now and then even with tongue-biting and often with micturition.

His m. ep. has now lasted for seventeen years in spite of antispasmodics. His seizures, occurring some few times a year, were always induced by listening to or remembering music. In the course of years his mental state has been a little reduced, but still he is able to look after his business.

Admitted to the Södra Sjukhuset, Stockholm, in February 1949 he revealed no neurological abnormalities. His psychic reactions as well were normal except for his memory which had become less retentive. X-ray of the skull was normal. Encephalography showed a slight dilatation of the left ventricular system, but left-sided angiography displayed a normal distribution of the brain vessels.

Two years ago Dr. Frey by means of EEG found focal abnormalities from the left temporal region induced by music. One year ago Dr. Holmberg by EEG only demonstrated a moderate general dysrhythmia. While the "Air on the G-string" by Johann Sebastian Bach was played for him the music affected neither the curves nor the patient. Then a record with Schubert's unfinished symphony, the second movement was put on. During its first mezzoforte part irregular high voltage 4-5 c/sec. waves appeared in the EEG from the left pre- and postcentral areas; and as the vigorous forte part followed, he had a typical general grand mal lasting for two minutes.

Recently at the Södra Sjukhuset in 1949, EEG only revealed a general rather pronounced dysrhythmia, but the earlier experiments with music were not repeated.

I saw the patient in 1942 and in April 1949, on which occasion I questioned his relatives for further details concerning his seizures. They explained that he was less apt to have his convulsions when he was eagerly occupied. On the other hand attacks were more easily induced by music when he was under stress. All his attacks came suddenly without any warnings, such as for instance a change in behaviour, respiration, face-colour, pupil-size or mood.

No impairment could be observed in his mental state during the last seven years.

Comment: This case of m. ep. seems to display both a definite psychogenesis and a close parallel to other forms of reflex-epilepsy. The diagnosis is certain, based upon a well elucidated

case-history, combined with clinical and experimental analysis exposing a hypothalamic and parietal epileptogenic process. The case therefore seems useful as a brick in the psychosomatic bridge between "organic" and "psychogenic" brain diseases.

DISCUSSION

Musicogenic epilepsy is a very rare disease, but closely related to other known forms of reflex-epilepsy. Experimentally epileptic seizures may for instance be induced by irritating the retinae with flashes of light. Clinically I have seen a patient getting her first Jacksonian attack in the moment when a too tight plaster bandage was removed from her ankle the morning after an orthopedic operation. The bandage caused the patient great pains in her foot, and she had no sleep at all during the night. The two cases mentioned display the process of a pathological facilitation in the neurones of the brain, carried on so long and so intensely that transient or lasting epileptogenic processes may arise.

Afterall, the cerebral hemisphere and especially the temporal and parietal lobe must be a necessary link in the neuropathological system of m. ep., but the centres in the hypothalamus controlling our emotions are of equal importance. M. ep. therefore may as well be called emotional epilepsy.

Until now no EEG investigations have been published of early cases of m. ep. In these cases one might expect by means of nasopharyngeal leads to find high voltage, slow potentials from the diencephalon alone. In cases of older date the EEG has constantly displayed a general dysrhythmia and during the paroxysms focal spikes or slow potentials starting from the parietal or temporal lobe and spreading with general spike-potentials all over the cortex, as the seizure evolved.

This accords well with our clinical experiences, where after a lapse of some weeks or months local cortical dysrhythmia

following e.g. a trauma of the head, will spread all over the brain cortex.

The four new cases of m. ep. here mentioned represent a cryptogenic, an arteriosclerotic, a traumatic, and a psychogenic origin, without any differences in the symptoms. This again goes well with the old clinical experience that neither focal symptoms nor an analysis of the attacks are able to tell us the etiology of the epilepsy.

Epilepsy plays the entire register of pathological processes possible in the brain. Kinnier-Wilsons paradox; "no such disease as epilepsy exists or can exist!" holds good of m. ep., too.

However rare m. ep. may be, it is useful in throwing light upon the pathogenesis of ordinary epilepsy. Unfortunately in the traumatic case mentioned, a total elimination of the traumatic process in the right temporal lobe, which to this left-handed man represented the primary epileptogenic focus, was impossible. But even if it had been possible totally to remove his cerebral scar, etc., it is uncertain whether he could have been completely cured as the operation was performed several years after his first musicogenic convulsion and the hypothalamus as well as the rest of the gray matter of the brain had been "epilepticised".

The earliest possible diagnosis and quickest practicable institution of the treatment are our best weapons in the fight against musicogenic as well as against any other form of epilepsy.

SUMMARY

(1) A survey is given of the literature on musicogenic epilepsy and the twenty-three cases published since 1884.

(2) Four new cases from Sweden and Denmark with different etiology are reported.

(3) Of these a traumatic case was the first case of m. ep. hitherto operated on. A typical traumatic process in the temporal pole was found by Dr. Busch at the operation.

(4) The pathogenesis of m. ep. is revised and it is shown that this rare form of epilepsy only differs from other forms of reflex epilepsy by its inducement by music.

My best thanks to Richard Eeg-Olofsson, M.D., Stockholm, and to the Chief Physicians of the neurosurgical department at the Södra Sjukhuset and at the Rigshospital for their kind assistance and valuable share in this article.

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Effect of Avertin and Citodan (Sodium Evipan) on the Cerebrospinal Fluid Pressure

By

P. TAARNHØJ

As soon as avertin had been introduced as an anæsthetic in neurosurgery it was noticed that, unlike ether, it did not raise the intracranial pressure to the extent of causing difficulties during the operation. In this respect the difference between avertin and ether was so striking that most neurosurgeons anticipated that avertin would be without any effect at all on the intracranial pressure (*Malmros*) and others even thought that it lowered the pressure (*Dott*). In 1931 *Gardner & Lamb*, however, reported increase in intracranial pressure during avertin anæsthesia. Studying 6 cases they found an increase in the pressure of about 100 mm. of water. *Butler* and *Horsley*, on the other hand, found that barbiturate, such as evipan (evipal, nembutal etc.) lowered the intracranial pressure by about 50 mm. of water.

In the Department of Neurosurgery of the University Hospital in Copenhagen the anæsthetics of choice are a combined barbiturate-avertin anæsthesia or pure barbiturate anæsthesia. It was therefore felt desirable to study the intracranial pressure during these forms of anæsthesia, especially as diagnostic puncture of the subarachnoid space or the ventricles is often performed under anæsthesia, and measurements of the pressure constitute an essential link of these examinations.

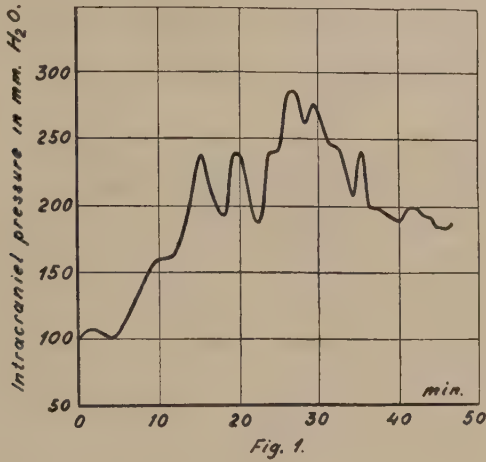
When avertin is used, the patient receives luminal, 30 cg., by mouth on the evening before the operation. The next morning an injection of luminal, 20 cg., is given and immediately before the anæsthesia pantopon, 3 cg. The procedure is to administer the avertin, by rectum, 80-100 mg. per kg. body weight with the patient lying on his right side. The anæsthetic is administered for half an hour, but usually the patient will be unconscious already when part of it has been given (*Busch & Olivecrona*).

The intracranial pressure was ascertained by measuring the cerebrospinal fluid pressure following lumbar puncture with the patient on his right side and the head level with the spinal canal. The needle was introduced before the anæsthesia and connected with a metal manometer by an air-filled rubber tube, and the pressure was read every minute. The subjects chosen were patients undergoing operation for herniation of the nucleus pulposus. They were all quiet, although they of course made minor movements before falling asleep, movements which easily might cause alterations in the lumbar pressure, as each centimetre the head was raised or lowered meant a change in the lumbar pressure of nearly 10 mm. of water.

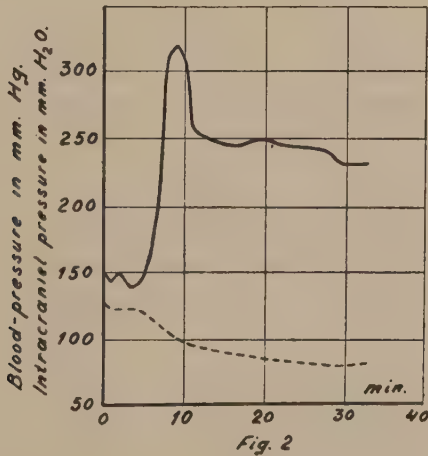
A group of 8 patients were studied during avertin anæsthesia. In one of them measurements were also made of the blood pressure (Fig. 2) which in our experience always falls somewhat during this form of anæsthesia. In another case (Fig. 3) the skin temperature on the feet was measured. Regrettably, I had only a maximum thermometer, so that I could only record raised, not lowered temperature.

It will be seen from the graphs (Figs. 1-4) that the results all point into the same direction. In the horizontal position the lumbar pressure was about 150 mm. of water in the majority of cases. Within the first 5 minutes the pressure began rising quite steadily, reaching maximum values about 20 minutes after the anæsthetic was started, and about the same time most of the patients had become unconscious. As the anæsthesia deepens there is a slight fall, usually about 50 mm. of water, possibly because the

patient is recovering from a stage of excitement which, however, is not manifest clinically. No measurements were made of the



cerebrospinal fluid pressure at later stages of the anæsthesia and when the patients returned to consciousness, as they were moved to the operating table as soon as the anæsthesia was sufficiently



deep. Major, sudden alterations in the pressure were usually due to changes in position, as even slight rotations could effect considerable changes in the level of the needle in relation to the head.

In one case the skin temperature on the foot was measured. Fig. 3 shows a rather steep rise some time after the anæsthetic was started. Possibly the temperature began to rise at an earlier juncture, but as mentioned above I had only a maximum thermometer which did not record temperatures below the horizontal part of the graph.

In another case the blood pressure was measured (Fig. 2). It was found to fall from 130 to 80 mm. This fall occurred almost simultaneously with the rise in intracranial pressure.

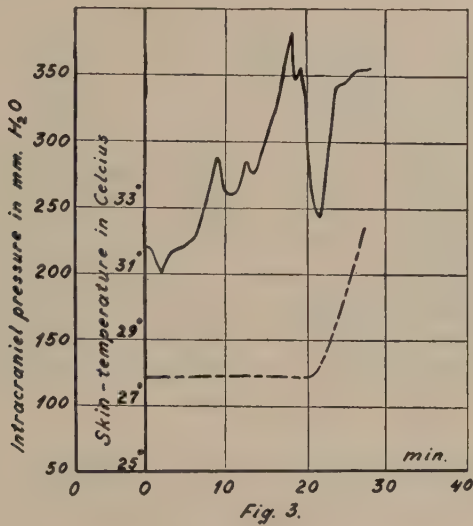
Furthermore, the intracranial pressure was measured in 7 patients under citodan (evipal, evipan) anæsthesia (Figs. 5-8). Like the former group, these patients had also received luminal, 30 cg., by mouth on the preceding night, 20 cg. intramuscularly on the same day, and pantopon, 3 cg., immediately before the anæsthesia.

This group is made up of 7 patients undergoing frontal lobotomy because of psychic disturbances. The intracranial pressure was measured by suboccipital puncture with the patients lying on their left side. As the effects of citodan are much more rapid than those of avertin, only 15 seconds were allowed to pass between the readings. Citodan was administered intravenously, quite slowly, $\frac{1}{2}$ cc. at a time, except in one case when it was given more quickly because the patient was excited. As a rule unconsciousness sets in quickly, but one patient (Fig. 8) hardly slept at all, even when she had received 10 cc. (10 cc. = 1 g.).

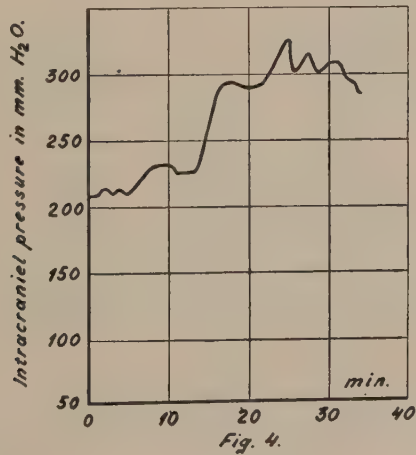
In 6 instances the intracranial pressure increased quite steadily, as will be seen from the graphs, the smallest increase being 60 mm. and the highest 135 mm. of water. In the case of an extremely excited patient who hardly slept at all after 10 cc. of citodan (Fig. 8) the pressure first fell from 220 mm. to 130 mm. in order to increase again to 250 mm. of water. Perhaps the high initial pressure was due to the excitement. When she had received the citodan, the pressure first dropped to normal values, because she quieted down, in order to increase again because of the anæsthetic.

In all the cases the blood pressure during the anæsthesia

exhibited a constant fall, usually to about 80 mm. of Hg. This decrease occurred at a rather early stage of the anæsthesia, as a rule somewhat before the intracranial pressure began to rise.

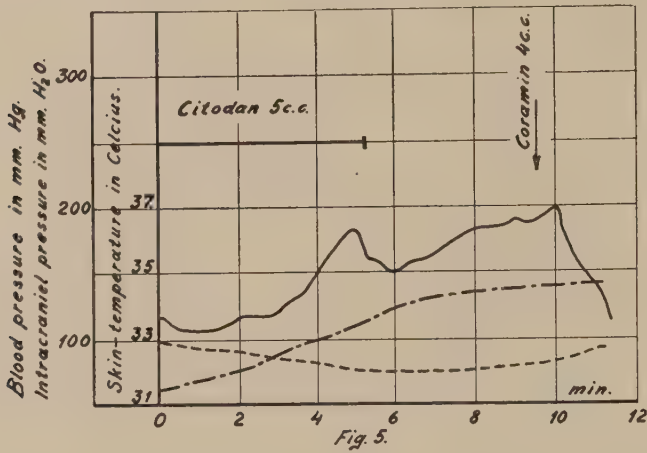


The skin temperature on the feet was measured in 5 cases who showed an even rise (Figs. 5 and 7).

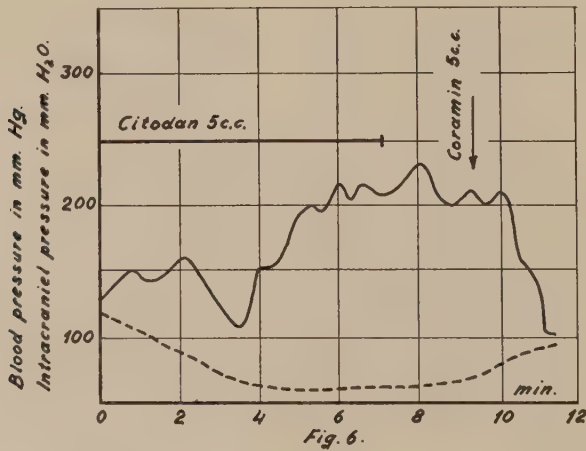


When the patients had been unconscious for some time, they were brought back to consciousness by an intravenous injection

of coramine, 4-5 cc. The effect was instantaneous in nearly all the cases, and there was a simultaneous increase in the blood



pressure and a rather steep decrease in the intracranial pressure to the values recorded before the anæsthesia.



DISCUSSION

While trying to find the reason for the rise in intracranial pressure during anæsthesia, one must not forget that the skull and the spinal canal make up an unyielding container, and therefore sudden alterations in the pressure can only be due to altera-

tions in the amount of the fluid in and around the central nervous system. These fluids are in practice the cerebrospinal fluid and

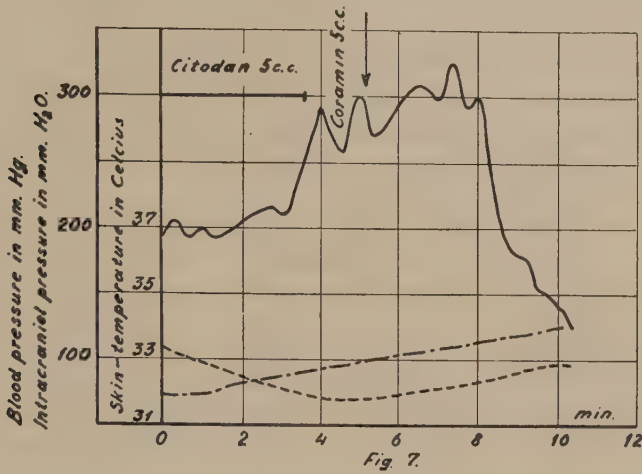


Fig. 7.

the blood. An increase in the intracranial pressure during anæsthesia may therefore be due either to an intracranial and

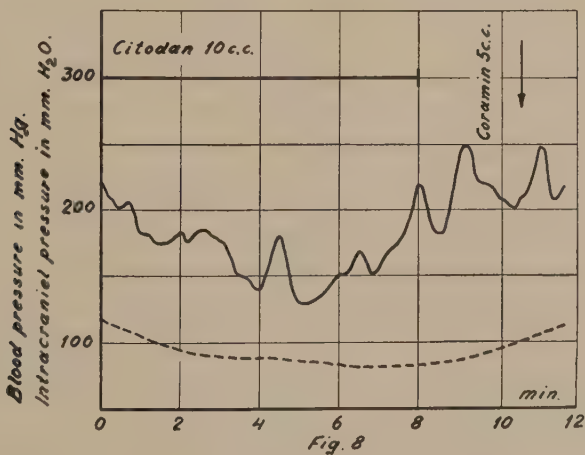


Fig. 8

intraspinal increase in the amount of the cerebrospinal fluid or of the blood or both.

Lindberg rejects the possibility that an increased pressure during anæsthesia should be due to an increased amount of cerebrospinal fluid, arguing that such alterations can hardly

take place as quickly as the increase in pressure. This argument cannot, however, stand close scrutiny. It must be borne in mind that from the point of view of physics the contents of the cranium and the spinal canal can be compared to water. In an unyielding container filled with water, an extremely slight increase in the amount is enough to cause marked increase in pressure, as the elasticity quotient of water is very low, i.e. $48 \cdot 10^{-6}$ atmosphere⁻¹. To a closed space filled with fluid one can apply the equation: $v = v_1 \cdot (1 - c \cdot p)$, where p is the increase in pressure measured in atmospheres, c the elasticity quotient of the fluid, v_1 the original volume and v the new volume.—The intracranial pressure is about 100 mm. of water = about $1/_{100}$ atmosphere. Under anæsthesia the pressure will rise approximately by a further 100 mm. = about $1/_{100}$ atmosphere. Roughly, the contents of the skull and spinal canal may be assumed to be 1500 cc. If the compression taking place during the increase in pressure under anæsthesia is called y cc., we have the equation: $1500 - y = 1500 \cdot (1 - 48 \cdot 10^{-6} \cdot 1/_{100})$, i.e. $y = \text{about } 1/_{1000}$ cc. In other words, an increase of only about $1/_{1000}$ cc. in the cerebrospinal fluid is required during the rise in pressure to effect a rise from 100 mm. to 200 mm. of water, and this is well within the range of possibility. Such a small increase in the amount of the cerebrospinal fluid will, however, probably immediately be compensated for by a corresponding alteration in the amount of blood due to venous compression. Moreover, there is a possibility that part of the cerebrospinal fluid may ooze out along nerve sheaths etc. In spite of this incorrect argument *Lindberg* may therefore be right in stating that the explanation of the increased pressure is to be sought in the vascular system.

Obviously, the pressure in the cortical veins must be higher than the intracranial pressure, as the thin-walled vessels cannot stand major external excess pressure, especially in their course through the subdural space where they are not attached to or supported by the surrounding tissues. As the cerebrospinal pressure is about 100 mm. of water = about 8 mm. of Hg. the venous

pressure is ≥ 8 mm. of Hg. This accords well with *Mosso's* finding that the pressure in the sinus sagittalis superior is higher than the pressure in e.g. the great saphenous vein. On the other hand, the venous pressure can hardly be much higher than the cerebrospinal fluid pressure, as the former venous pressure must be lower than the capillary pressure, and the latter can be estimated approximately as follows: It is known that a diffusion takes place between the capillary contents and the surroundings. The force which keeps the blood in the capillaries is the colloid osmotic pressure of the blood, and in order that such diffusion may take place, the pressure in the capillaries in the arterial end must exceed the pressure of the surroundings by more than the colloid osmotic pressure of the blood which is 28 mm. of Hg., as no exudation can otherwise take place from the capillaries into the tissues. At the venous end, on the other hand, the diffusion is to the capillaries from the surrounding tissues, and therefore the pressure in the capillaries must not exceed that of the surroundings by 28 mm. By the pressure in the surroundings is meant the intercellular pressure in the brain which probably is equal to the cerebrospinal fluid pressure. Accordingly, the capillary pressure cannot exceed the cerebrospinal pressure by 28 mm. of Hg., and as the venous pressure must be somewhat lower than the capillary pressure due to the decrease of pressure in the venules, it cannot be much higher than the cerebrospinal fluid pressure. Consequently, the pressure in the cortical veins must be slightly, but not much higher than the cerebrospinal fluid pressure.

Finally, it must be pointed out that the fluctuations which may take place in the amount of cerebrospinal fluid during the experiments in question, especially during the brief citodan anæsthesia, cannot amount to much when compared with the fluctuations possible in the amount of blood. The total amount of cerebrospinal fluid in the cranium is only about 100 cc., so fluctuations probably amount to only a few cc. When also considering that the cranium and the spinal canal are an unyielding

space and that the elasticity quotient of water is so low that compression of the cerebrospinal fluid is only possible to a very slight extent, the total amount of blood in the cranium and spinal canal must remain approximately constant during the time of the experiment.

This suggests the following theory to explain the rise in intracranial pressure under avertin and citodan anæsthesia.

As apparent from the rise in temperature recorded in the feet, arteriolar dilatation takes place in this site, a dilatation which probably also applies to the cerebral arterioles. This phenomenon is the primary cause of the fall in blood pressure. In the cranium this dilatation will cause venous compression, as the amount of blood is approximately constant, as already mentioned. In consequence, the pressure in the veins increases, and this accords with *Mosso's* studies of the pressure in the sinus sagittalis superior under anæsthesia. Increased venous pressure must result in increased cerebrospinal fluid pressure, as it has been shown that the two go together. The reason why the cerebrospinal fluid pressure increases is probably that the absorption of the cerebrospinal fluid is to be effected at a higher venous pressure.

SUMMARY

The writer has studied the cerebrospinal fluid pressure in 8 subjects under avertin and 7 under citodan (sodium evipan) anæsthesia. In all the cases the pressure rose during the anæsthesia. Only in one case of citodan anæsthesia, that of a patient who had been very excited just before the anæsthesia, there was first a decrease and then an increase in the pressure. In addition, some measurements were made of the blood pressure, which showed a constant fall, and the skin temperature which was found to rise. The 7 patients submitted to citodan anæsthesia were brought back to consciousness with coramine, and the values returned to the level recorded before the anæsthesia. Finally, the writer suggests a theory to explain the rise in intracranial pressure found during anæsthesia.

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Notes on the Importance of the Occipital Lobes in a Case of Schizophrenia

Experience with a case of bilateral occipital leucotomy.

By

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The relationship between the cortical and subcortical centres have been studied in various ways, especially by attempting a registration of the association between the basal ganglia and the cortex (4 & 5). Cannon (3) has studied the relationship between the diencephalon and the cerebral cortex in order to explain the emotions. He has also tried to study the affective component of the personality and its relationship to the hypothalamus. Lesions in these regions have been studied also by Wheatly (14) and by Alpers (1).

The importance of the frontal lobes seen in relation to the emotional part of the personality has been discussed by Freeman and Watts (8). These authors emphasize the importance of the impulses which pass between the frontal lobes and the thalamus and their view is at the present time generally accepted also by other authors who have studied these special questions (6). It has not been definitely pointed out which of the frontothalamic fibres are of especial importance in this connection. Isolated partial frontal disconnection of the fibres (9) have been studied and leave the impression that the basal frontal fibres have a predominating function on the emotions (10).

Among other parts of the central nervous system which are likely to be of importance for the characterological changes in psychiatric patients, the temporal lobes must be considered as possible sources of symptoms. The complex types of psychic epileptic aura and epileptic fits which follow lesions in the



Fig. 1.

temporal lobes, make this part of the central nervous system a possible anatomical source of psychosis. Experience has shown that the residual phenomena following amputation of the temporal lobes causes less changes of the personality than is the case as long as the temporal lobes are a site of pathological alterations. From an anatomical point of view the temporal lobes are especially interesting inasmuch as there are no direct connecting fibres from the thalamus apart from the small auditive field in the first temporal gyrus (13). This indicates that the impulses to the temporal lobes arrive from different other fields, making the temporal lobes a region of association par excellence (2). Deeply

located in the temporal lobes are structures of little known functions, such as the uncus and the hippocampus. Presumably these regions are connected to the old olfactory cortex, but there is considerable doubt on this point because stimulations of the olfactory bulb do not result in corresponding electric activity of the hippocampus or the nucleus amygdalus (7).

Experiments with monkeys have shown that bilateral amputation of the temporal lobes provokes a picture of visual agnosia or psychic blindness associated with considerable changes of the emotional personality. The emotional reactions undergo changes in such a way that such vocal motor reactions as are usually associated with anxiety and rage lose their irritating effect. This is not seen after unilateral extirpation of the temporal lobe. It has been shown that such pacification also follows when one temporal lobe is removed after previous bilateral extirpation of the frontal lobes. In order to make the extirpation of the temporal lobes effective the hippocampus must also be removed.

The review of the anatomical and psychological data which has been given above, makes it easy to understand that the temporal lobes have been looked upon with great interest as a possible location for leucotomy in humans. Leucotomy of this type has been carried out by Obrador (12) on a schizophrenic patient suffering from marked hallucinations, predominantly of an auditive character. Apart from provoking a verbal agnosia, the operation resulted in a mental reaction which was very like the one usually seen to follow frontal leucotomy in the first postoperative period. However, after a week's time, the patient began to be troubled by the same symptoms, inclusive of the auditive hallucinations, as had been present before the operation. The incision in the brain had been placed immediately in front of the temporal horn up to the Sylvian fissure and was about 4½ cm. deep. About 3 weeks later the usual bilateral frontal leucotomy was carried out, followed by the usual kind of mental reactions. Observations 4 weeks after this interference showed

that the patient at that time had lost his anxiety and the abnormal mental tension.

A similar operation was carried out also on another schizophrenic patient, on whom previously frontal leucotomy had been carried out without any noticeable effect.

Thus the impression remains that the temporal leucotomy is followed by little or no improvement in the symptoms, the removal of which is its primary aim.

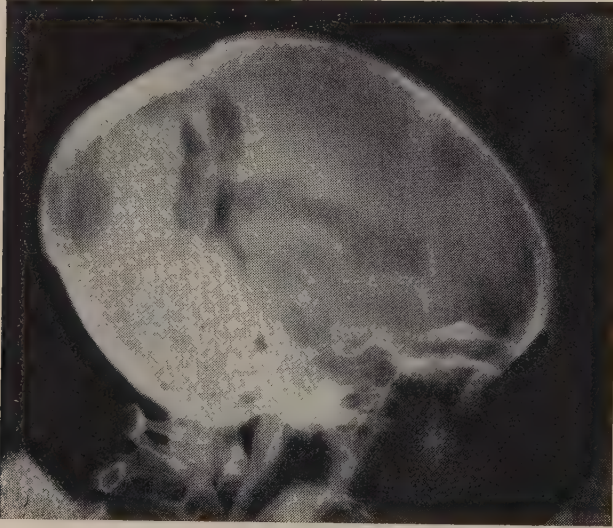


Fig. 2.

Pimenta et al. have sectioned the longitudinal fronto-occipital fibers in the parietal region in 22 cases, 19 of which were schizophrenics. The section was carried out by a technique similar to the one used for ventriculography with the primary aim of interrupting the fibers of the corpus callosum. The patients showed little or no improvement (15).

His operations differ fundamentally from the one carried out in the case to be published here, in as much as the section used by Pimenta comprised only a small region superior to the lateral ventricle, while the section I have carried out in my case completely interrupted the white matter throughout the parietal region down to the tentorium of the cerebellum.

The surgical treatment of mental diseases is under constant development and it is far from having reached a satisfactory development. It is necessary to continue the study of the various types of possible operations and the various regions of the brain on which the operations possibly should be carried out in order to remove the symptoms which are of the greatest importance to the patient. One region of the brain on which it has been difficult to carry out operations, is the occipital lobe inasmuch

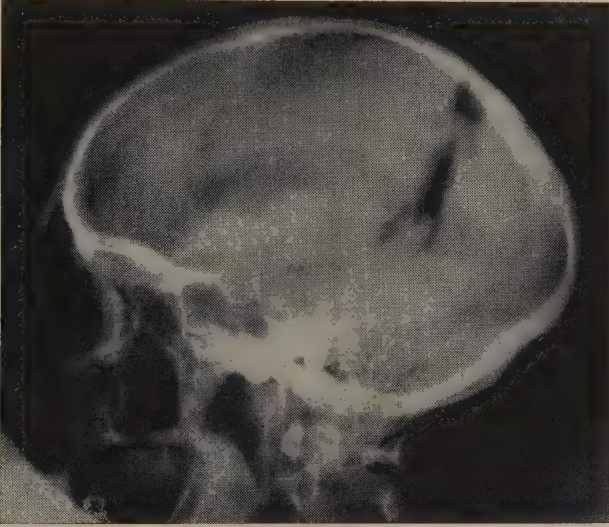


Fig. 3.

as destruction of the visual fibres to field 17 is a necessary consequence of any interference in this part of the brain. In order to make clear if the occipital lobes are important or not in connection with mental diseases, I have carried out bilateral occipital leucotomy in a schizophrenic patient.

During my work I have had the privilege of the cooperation of Dr. H. H. Dedichen as far as the psychiatric studies are concerned.

Case report: The patient was a man, 30 years old, who had suffered from occasional epileptic fits since he was 15 years old. Since 1941 this patient had developed doubtless signs of schizophrenia. The hallucinated patient imagined that he could hear the voice of Our Lord, telling him to destroy both his eyes.

If so, he would get rid of his epileptic fits and later on he would regain his visual power. The schizophrenic patient followed this command. He destroyed both his eyes resulting in complete blindness. In course of the years the patient developed considerable dementia, making detailed psychiatric examinations difficult and unsatisfactory. On the 20th of February 1948 I carried out a bilateral occipital leucotomy. The pictures which are shown here, explain better than any words the location of the incision. The pictures have been taken after encephalography, 8 days after the operation. The incision comprises as far as possible all white matter. After the operation the patient remained hallucinated as before. He assumed an autistic attitude and it was perhaps even more difficult to obtain contact with him than it had been before the operation. It should be stressed that the frequency of the epileptic fits as well as their type remained unchanged by this operation. After the patient had been under psychiatric observation for more than six months without displaying improvement as far as the psychic condition was concerned, the usual type of a bifrontal leucotomy was carried out on September 21st, 1948. For this operation I followed the usual technique of Freeman and Watts. This second operation resulted in no definite improvement or change of his psychic condition. The patient is still in the asylum under the supervision of Dr. Dedichen for further psychiatric studies. It is difficult to obtain communication with this patient. He remains autistic. The case will be published in detail when the necessary anatomical basis has been obtained.

This preliminary report, although incomplete, may perhaps be of some interest as no similar operation has ever been carried out before, as far as I can see from the literature. The experience with this case shows that the disconnection of both occipital lobes has no noticeable influence as far as can be judged from the psychiatric observations. It is also of importance to stress that it has not been possible to point out agnostic or other neurological phenomena in spite of such massive lesion in this part of the brain. The operation has had no influence on his epilepsy.

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Angioma of the Spinal Cord¹

By

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Angioma of the spinal cord is one of the lesions which in most cases remain undetected until on the operating table or in the post-mortem room (*Globus & Doshay*, 1929). This is primarily due to its extremely changing course which makes it impossible to set up definite criteria for the clinical diagnosis.

In reporting the 4 angiomas of the spinal cord diagnosed in this laboratory during the period 1935-48, the writer does not pretend to contribute essentially to the future clinical diagnosis of the lesion. They are, however, of interest, as the first one was complicated by a monstrous hæmorrhage, the second co-existed with another kind of tumour, and all 4 aptly illustrate how capricious may be the course of angioma.

Case I. N. P. L. (No. 59/48).—Male, aged 58. Admitted for the first time to Kommunehospital, Neurological Department, in 1942. History of pain of varying intensity in the loin and back of about 2 years' standing. At the same time gradually increasing paresis of the right leg and paræsthesiæ of the foot.—Obj. exam. revealed loss of abdominal reflexes. Hypæsthesia-hypalgesia on the outside of the right lower limb and of the right 4th-7th thoracic segments. Mild paresis of the right ankle and mild spasticity of the right lower limb. On lumbar puncture, Queckenstedt's test showed rise and fall. Cells: 2 lymphocytes per cmm., protein content 83 mg. per cent. W.r. —. Blood pressure 180/120. Other laboratory tests showed no abnormalities.

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X-ray of the spine showed spondylosis of the lumbar and the lowest dorsal vertebræ. The condition improved after bed rest and physical treatment.

During the subsequent year the condition remained practically unchanged, but in 1945 the pain in the loin returned and there was now also shooting pain in the left leg. Admitted to Kommunehospital, Department of Physical Therapy, where the objective neurological findings almost corresponded to those observed at the Neurological Department the first time. Lumbar puncture revealed: 0 cell, protein content 116 mg. per cent.

The power in both legs was steadily decreasing, and gradually transient sphincter disturbances set in. Moreover, there was exacerbation of the pains in the back and loin and gradually violent pain radiated down into the legs. In 1948 the patient re-entered the Neurological Department, where objective examination showed mild atrophy of the muscles of the right hand. Hypalgesia below the horizontal line through the papilla on the right and below the costal border on the left side. The sense of touch was diminished caudally to the ensiform process. Uncertain postural sense in the toes. Spastic paralysis of both legs.—Lumbar puncture showed a rise, but no fall in Queckenstedt's test. The fluid was lemon-coloured and clear. No cells, protein content 675 mg. per cent. Cisternal fluid: 1 cell per cmm., protein content 50 mg. per cent. On suboccipital myelography the contrast medium stopped on a level with the 4th cervical vertebra.

The patient was then transferred to Rigshospitalet, Department of Neurosurgery, where laminectomy was performed of the 3rd-7th cervical vertebræ. The laminæ proved to be quite thin and the spinal canal showed increased width. The dura was tense; pulsation was only found down to the level of the 3rd cervical vertebra. In the cord there was a bluish cyst-like formation extending from the 3rd to the 5th cervical vert. The cyst contained a clear yellowish fluid. No mural tumour was found. After the operation the patient was moved back to Kommunehospital, Neurological Department, where he died with symptoms of pneumonia slightly more than 2 months after the operation.

Post-mortem findings: Bronchopneumonia. Mucopurulent bronchitis. Pulmonary oedema. Cystitis. There were no other abnormalities outside the central nervous system, especially no vascular anomalies. Examination of the central nervous system showed no gross abnormality of the brain. The spinal cord, on the other hand, was extremely swollen, except on a level with the remains of the cyst-like formation in the cervical region. Its entire surface showed tortuous, but mostly thin vessels. Approximately on a level with the 4th-6th thor. vert. there was an angiomatous formation with numerous, mainly small vessels; in this site there was some fresh hæmorrhage of a moderate subarachnoid extent. Horizontal section through the cord showed on a level with the angiomatous area a central, more recent hæmorrhage surrounded by a quite thin border of nervous tissue. Cranially as well as caudally to the angioma there was a yellowish, gelatinous mass which extended up to the

cysts in the cervical region and down through the entire lumbar and sacral region, decreasing, however, distinctly downwards. It was localized predominantly in the grey matter, but in the vicinity of the angioma it also involved the white matter.

Micr. exam.: In preparations from transversé sections of the cord on a level with the 5th thor. vert. there was a hæmorrhage almost throughout the entire transverse section. In the periphery there was only a thin border of white matter with degenerated myelin sheaths; no nerve cells. The normal pattern

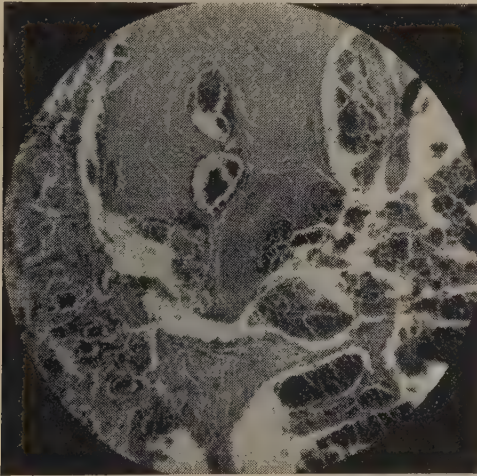


Fig. 1.

Case I. Section of the angioma showing hæmorrhage.

Hæmatoxylin-eosin, $\times 75$.

of the cord was obliterated and so was the anterior median fissure. At the site of the right anterior horn there was a number of major and minor blood-filled vascular lumina with interposed glial tissue in a state of partial breakdown (Fig. 1). The thickness of the vascular walls varied somewhat; a few reminded of atypical arteries, others of atypical veins. A few vessels had ruptured and were thus apparently the origin of the hæmorrhage. In elastin-stained preparations several, non-ruptured vessels showed an incomplete elastica interna. The vascular anomaly was connected with the fairly ample arteries and veins on the surface of the cord. The vascular walls in and outside the angioma showed a marked tendency to hyalinization. Transverse sections from the cervical cord on a level with the remains of the cyst only held a rather small quantity of white matter with abundant glia; everywhere the myelin sheaths were in a state of marked degeneration; no nerve cells were observed. In this region there was no angiomatous formation. The lumbar and sacral cord showed evidence of previous hæmorrhage, mainly localized in the central area of the grey matter. The extent of the hæmorrhage diminished gradually caudally in

the cord. Particularly in the lowest segments there were nerve cells in the anterior as well as posterior horns. A large number of these cells were, however, chromophobe, others sclerotic; most of them held lipochromic pigment. In the white matter there was extensive degeneration of the myelin sheaths. In the uppermost lumbar segments a number of major and minor vessels with walls of varying thickness localized in the right anterior funiculus and horn. This lesion was, however, of a very slight extent compared with that observed in the thoracic segments.

In the pons and the medulla oblongata there were small accumulations of vessels in places, on the surface as well as in a few places in the parenchyma. Here, too, the vessels were somewhat hyalinized and were here and there surrounded by small hæmorrhages. Other parts of the brain failed to exhibit any definite abnormalities.

Hist. diagnosis: Arterio-venous angioma of the thoracic cord with hæmorrhage.

Summary of the Case: Male, aged 58. Pain, disturbances of sensibility, and pareses of 8 years' standing, at the outset affecting mainly the right lower limb, gradually also the left, the sphincters, trunk, and at last the right upper limb. Post-mortem examination showed an arterio-venous angioma on a level with the 4th-6th thoracic vertebræ and intraspinal hæmorrhage extending up to the cervical and down to the sacral region.

Case II. H. J. (No. 7/45). Male, aged 57. Admitted to Kommunehospitalet, Neurological Department, in 1925. Radiating pain in the right lower limb of a few months' standing. Now and then paræsthesiæ in the right foot. At times occipital pain. Obj. exam.: No neurological signs. The symptoms yielded to physical treatment.

In 1928 the patient was re-admitted to the Neurological Department as the occipital pain persisted and had lately grown more severe. Now the pains were throbbing, radiating to the vertex as well as down the back, independently of temperature and weather. This time it was not either possible to demonstrate any neurological abnormalities, but myalgic changes were found in the nuchal muscles. Again improvement after physical treatment.

Re-admitted in 1943. Stated that the occipital pain had gradually subsided entirely. During the year preceding this admission there had been pain in the loin, radiating into the left thigh. The left leg felt heavy and dragged in walking. Difficulty in urination of some months' standing.—Obj. exam.: Abdominal reflexes lost. Lower limbs slightly spastic with preponderance of left-sided reflexes. Bilateral Babinski. Hypæsthesia-hypalgesia on left leg; no definite pareses. Spinal fluid natural. Cystometry: Extremely reduced action of the detrusor urinæ.

Ten months later the patient was admitted to Kommunehospital, Surgical Department V, with retention of urine and died in a few days.

Post-mortem findings: Pulmonary oedema. Cystitis. The brain did not show any macroscopic abnormalities, but in the spinal cord the normal pattern was obliterated in the cervical region, where a centrally situated, granulated,

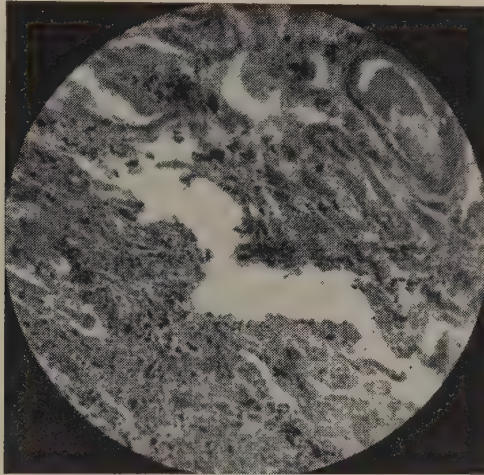


Fig. 2.

Case II. Section of the angioma. In the top left-hand corner strands of ependymal cells. Hæmatoxylin-eosin. $\times 75$.

brownish, soft tumour occupied several cm. of the cord's length. The thoracic and lumbar cord was normal on gross inspection.

Micr. exam. of the cervical cord showed two tumours, one of which was an angioma with hæmorrhages which apparently had occurred a varying length of time ago, as there were partly well-preserved blood corpuscles, partly blood pigment engulfed by macrophages. There were both arteries and veins and smaller vessels in between (Fig. 2). The tumour appeared to rise from the vessels in the anterior median fissure with which it was intimately connected. The imbibition of blood could be traced as far as the anterior part of the cord at the site of the anterior horn. The angioma showed remains of ependymal lining from the central canal in the form of isolated strands of ependymal cells around certain areas of the tumour.

The other growth was made up of numerous, chiefly hyalinized blood vessels around which typical tumour cells were radially disposed (Fig. 3). The cells were partly oblong, partly polygonal with eccentric nuclei; many of them sent long filamentous extensions towards the vessels. The surrounding medullary tissue was compressed and showed perivascular round-cell infiltration. Most of the myelin sheaths were distinctly degenerated; all the nerve cells had perished. In the thoracic and lumbar segments of the cord there was degener-

ation of the myelin sheaths, particularly of the posterior funiculi. In the anterior horns the nerve cells were relatively well-preserved, but swollen and with the remnants of tigroid peripherally.

Hist. diagnosis: Angioma and ependymoma of the cervical cord with hæmorrhage and degeneration. (sd. Erna Christensen).

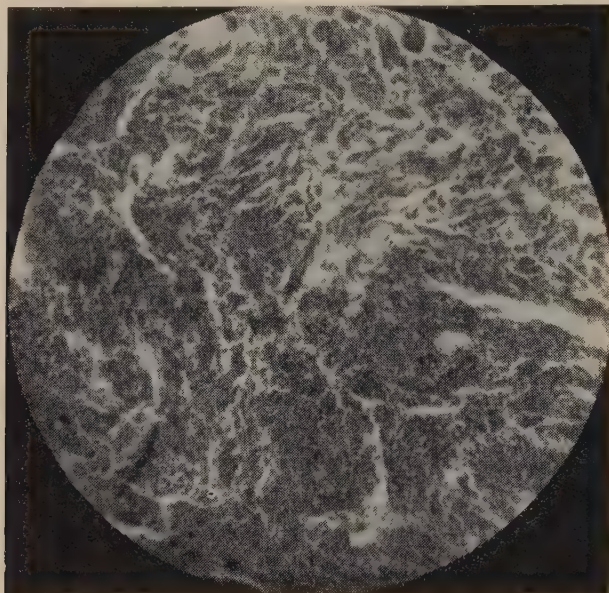


Fig. 3.

Case II. Section of the ependymoma. Hæmatoxylin-eosin. $\times 75$.

Summary of the Case: Male, aged 57. Symptoms of 20 years' standing. At the outset pain in the back of the head and in the right lower limb, gradually followed by spasticity of the lower limbs and sphincter disturbances. Post-mortem examination showed an angioma and an ependymoma in the cervical region.

Case III. O. J. (No. 17/42). Male, aged 57. Admitted to Kommunehospital, Neurological Department, in 1942. History of impotence for the last 5-6 years, difficulty in urination for a couple of years, and mild paresis of the left foot for slightly more than 2 years. During the last 18 months backache, especially in the loin, not radiating. During the last year or so paresis of the left hand and for the last few months loss of sensibility in both legs.—Obj. exam.: Direct tenderness of lumbar column. Paresis of abdominal muscles, abdominal reflexes absent. Hypæsthesia-hypalgesia caudally to the umbilicus. Mild, spastic paresis of both lower limbs and mild atrophy of the left quadriceps.—Lumbar puncture

revealed neither rise nor fall in Queckenstedt's test. Cells: 1 lymphocyte per cmm., protein content 200 mg. per cent.—X-ray of the spine showed nothing abnormal apart from mild spondylosis.

The patient was transferred to Rigshospitalet, Department of Neurosurgery, where laminectomy (7th cervical-4th thoracic vert.) showed that the cord was dilated, fluctuating, and whitish yellow with only a few vessels on the surface. On the other hand, there was a distinct arachnoiditic reaction. As the puncture yielded no fluid, it was thought to be a case of glioma, and further interventions were abandoned in view of the patient's poor general condition. After the operation the patient followed an even downhill course. The retention of urine persisted and gradually led to infection of the urinary tract. A fortnight after the operation the patient died with symptoms of pneumonia.

Post-mortem findings: Bronchopneumonia. Pulmonary oedema. Acute cystitis.

No abnormalities in the brain. The lowest thoracic and uppermost lumbar segments of the spinal cord were swollen. The cut section showed a yellowish red tumour-like mass.

Micr. exam.: In the cervical cord there was typical degeneration of the posterior funiculi and the cerebellar lateral tracts. The thoracic cord segment was in a state of marked necrotic breakdown, showing numerous well-filled gitter cells, round cells and detritus. The tumour-like tissue proved to be made up of a malacic-necrotic area, the architectural markings were obscured and there were numerous gitter cells. The necrotic area also contained numerous densely arranged vessels, partly of a venous, partly of an arterial type, with an oblong, somewhat tortuous lumen. The vascular walls were in many instances thickened and hyalinized.

Hist. diagnosis: Angioma of the spinal cord. Necrosis of the spinal cord. (sd. Munch-Petersen).

Summary of the Case: Male, aged 57. A progressing spastic paresis of the lower limbs with sensory disturbances and sphincter disturbances of 5 years' standing. Obj. exam. revealed paresis of the abdominal muscles and a mild spastic paresis of the lower limbs with reduced sensibility below the umbilicus. Post-mortem examination showed an angioma in the lowest thoracic and the uppermost lumbar segments.

Case IV. A. L. (No. 12/41). Female, aged 60. Admitted to Kommunehospitalet, Neurological Department, in 1941. For the last 3-4 years increasing paresis of the right leg and left arm. During the last year incontinence of urine. Eight days prior to admission a sudden stiffness of both legs and spasm of the right. —Obj. exam.: Some atrophy of the muscles of the left hand, flaccid paresis of the distal part of the left upper limb. Paresis of the abdominal muscles; abdominal reflexes lost. Spastic paresis of both lower limbs. Sense of vibration

absent in right lower limb, reduced in the left-sided extremities. Hypæsthesia-hypalgesia and almost thermanæsthesia caudally to the 1st thor. segment. Lumbar puncture: Rise and fall in Queckenstedt's test. Cells: 7 lymphocytes per cmm., protein content 675 mg. per cent.—X-ray of the spine showed nothing abnormal. Urine infected. The patient followed an even downhill course and died in hyperpyrexia.

Post-mortem findings: Subchronic cystitis. Cirrhosis of the liver (Laënnec's type). Chronic hyperplasia of the spleen. Oesophageal varices.—Central nervous system: No focal lesions in the brain. In the medulla oblongata the architectural markings were almost quite obliterated; in the posterior part there was a brownish red discoloration, the size of a pea, with an irregular cavity in the centre. The central area of the cervical cord was filled with a mass, $1 \times 1\frac{1}{2}$ cm., resembling a blood clot. It was sharply demarcated from the medullary tissue, which presented itself as a narrow border around the pathological process. The markings were also obscured in those parts of the spinal cord which were immediately below the clot-like tissue. These changes could be traced, markedly decreasing it is true, even down to the thoracic segments.

Micr. exam.: Sections from the cervical cord showed marked necrosis and a number of old as well as rather fresh, fairly well-defined hæmorrhages. Very slight glial reaction. The necrosis and hæmorrhages were in the central area, showing a more well-preserved zone in the periphery. Abundant vascularization and proliferation of the vascular walls. This was particularly distinct in the preparations stained to set out the connective tissue. On the whole these preparations revealed the cavernoma-like nature of the tissue most distinctly. Sections from the area below the one described showed diffuse necrosis, but no hæmorrhage. In the thoracic and lumbar segments there was beginning degeneration of the pyramidal tracts, but otherwise nothing abnormal.

Hist. diagnosis: Cavernoma and hæmorrhage of the cervical cord. (sd. Munch-Petersen).

Summary of the Case: Female, aged 60. In the course of 3-4 years there had been a progressing spastic paraparesis inferior, paresis of the abdominal muscles and of the left upper limb. Marked hyperalbuminosis.—Post-mortem examination showed an angioma of the cervical cord with some hæmorrhage.

DISCUSSION

As regards the *clinical aspect* it applies to the cases reported above as to all such cases in general that the first, often vague symptoms fail to arouse a definite suspicion of angioma. In Case I the diagnosis on first admission was radiculomyelitis;

presumably there has also been a reactive inflammation of the leptomeninges (cf. Case III). Apparently, this is no uncommon phenomenon. Thus *Buckley* (1936) has reported a case of medullary angioma diagnosed clinically as meningomyelitis.—Even vaguer were the initial symptoms in Case II in which it was only possible to ascertain the presence of fibrositis, which had to be interpreted as a secondary phenomenon.

In the last two cases, however, the symptoms were so advanced on admission that it was realized that it must be a question of intraspinal tumour. As emphasized by *Globus & Doshay* (1929) it is, however, extremely difficult to discover the real nature of the tumour before the operation in patients of this category. *Wyburn-Mason* (1943) states that he has several times obtained help from kymograms made in the course of myelography and which at times showed pulsation synchronous with the heart beat on a level with the arrest of the contrast oil. In our Case I where the contrast oil was arrested by the intraspinal hæmorrhage and not by the angioma, such a procedure would not have led to a positive result.

Even at the time of operation it may be difficult to diagnose the angioma. In our Case I the cyst found upon laminectomy was interpreted as having arisen in an astrocytoma. This is not surprising, as there were no distinct vascular abnormalities on a level with the cyst. As no mural tumour was demonstrable, it was concluded that it must be a case of hæmatoma in a state of breakdown. The operation did not, however, afford any evidence of the origin of the hæmorrhage, as the laminectomy was made in the cervical region where the contrast oil was arrested, whereas the angioma later proved to have its site in the thoracic region. Case III was also interpreted as a glioma at the operation, as there was reactive arachnoiditis, thickening of the cord, and puncture yielded no fluid. As the patient's general condition was desolate, further interventions were not expected to lead to a favourable result, and nothing more was done to elucidate the nature of the affection.

From the point of view of *pathology*, interest has primarily centred in two problems, viz. the classifications of the vascular anomalies and the question as to whether or not angiomas are actual neoplasms. Secondly, interest has been devoted to the secondary changes which may attend these lesions, mainly the hæmorrhages and their extent.

The classification of vascular abnormalities in the central nervous system and particularly in the spinal cord has not yet been firmly established. Nearly every major paper on the subject brings its special classification, although several of them only differ on immaterial points (*Cushing & Bailey*, 1928; *Globus & Doshay*, 1929; *Bergstrand*, 1936; *Elsberg*, 1941; *Turner & Kernohan*, 1941; *Wolf*, 1941; *Wyburn-Mason*, 1943). One of the reasons why it is so difficult to make an adequate classification is that the materials are too small. For example, among *Wolf's* material of 253 intraspinal tumours there were only 5 angiomas of which only 1 was intraspinal and leptomeningeal. The largest material is the one reported by *Wyburn-Mason*, who collected 120 definite cases from the literature and added 67 of his own. He divides the vascular anomalies of the spinal cord into the following main groups:

A. *Abnormalities*. (1) Venous abnormalities, (2) arterio-venous angioma, (3) arterial anomalies, (4) syphilitic aneurysm of the spinal arteries, (5) teleangiectases, including so-called cavernomata or cavernous angiomata.

B. *True tumours*. (6) Hæmangioblastoma or hæmangio-endothelioma, (7) lymphangioma.

All 4 cases under discussion must be allocated to the group of arterio-venous angiomas in view of the large, dilated arteries and veins in the pia and the atypical vessels of arterial as well as venous type in the lesions proper. This also applies to Case IV, although the hæmorrhage and extensive necrosis in this case make the interpretation somewhat more difficult. The localization fits, too, as *Wyburn-Mason* found that arterio-venous angioma had two sites of predilection, viz. the posterior portion from

the seventh thoracic, to the upper lumbar segments, and the anterior portion of the cervical enlargement, whereas angioma racemosum venosum is only met with in the caudal part of the cord. Only Case I forms an exception to these sites of predilection, the lesion being in the upper half of the thoracic region.

It is not always easy to decide whether vascular anomalies of the spinal cord are neoplasms, malformations, or the result of congestion (*Antoni*, 1936). This problem is discussed even in the earliest papers on the subject, e.g. by *Hebold* (1885) who concluded that a medullary anomaly, which he described as being composed of small aneurysms, must be congenital.

The congenital origin of a large number of these pathological conditions is borne out by *Kadyi's* studies (1889), which revealed various degrees and several types of varices on the spinal cord veins even in healthy individuals. *Kadyi* therefore concluded that a careful study of larger series would disclose a gradual transition from normal conditions to extremely marked vascular changes. Even although *Turner & Kernohan* (1941) are inclined to believe that angiomas are primarily due to static or other functional circulatory disturbances, most recent authors agree with *Wolf* (1941), who states: Angiomas are at present considered by most pathologists to be developmental vascular anomalies, capable of subsequent alteration in size and character.

Among secondary changes which may attend these lesions, hæmorrhage is most important. Cases of this nature have been described amongst others by *Harman & Balck* (1900), *Lorenz* (1901), *Bang* (1921), *Buckley* (1936), *Teilum* (1937), *Pappenheim* (1938), *Farago* (1942), and *Wyburn-Mason* (1943). It is a characteristic feature that the hæmorrhage primarily involves the grey matter as demonstrated experimentally by *Goldscheider & Flatau* as early as 1897. This is also confirmed by our cases, although the hæmorrhage in Case I was so monstrous that it involved also the white matter on a level with the angioma and several segments on either side of it.

Our Case II exhibited a rather exceptional complication of the angioma, a typical ependymoma lying close to it. It is impossible to state with certainty whether these two pathological processes were related etiologically, but it is interesting to note that the part of the angioma reaching the central canal was lined with strands of ependymal cells. As apparent from what has been said above, the angioma must be presumed to be a congenital affection and may consequently have been present before the ependymoma. It is therefore theoretically possible that the angioma, while growing, has irritated the ependymal cells and thus been at any rate a contributory cause of their proliferative growth. In this connection it is not out of place to mention the old observation that the ependyma proliferates in cases of syringomyelia when the cavity reaches the central canal (*Spiller, 1907*).

As far as the *treatment* of angioma is concerned, it has been attempted to remove part of the vessels, to ligate the afferent or the efferent vessels. In addition, X-ray therapy has been widely used, in some instances after operation.

SUMMARY

A report of 4 cases of angioma of the spinal cord, one attended with a monstrous intraspinal hæmorrhage and another co-existing with an ependymoma adjacent to the angioma. All 4 cases are classified as arterio-venous angiomas.

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Cerebral Pedunculotomy for The Relief of Involuntary Movements

I. Hemiballismus.

By

A. EARL WALKER

That interruption of the corticospinal pathway will abolish the abnormal movements in athetosis, choreo-athetosis, hemiballismus and Parkinson's disease is well established by the experimental and clinical investigations of *Sachs* (9), *Foerster* (5), *Browder* (1), *Horsley* (6), *Bucy* (2), *Putnam* (7) and others. This interruption may be made at the cortex (2, 3, 5, 6, 8, 9), internal capsule (1), or spinal cord (7). When the abnormal movements are on the right side, an aphasia is likely to complicate the result of a left cortical excision. This undesirable sequela stimulated a search for a level at which the corticospinal tracts are relatively isolated, superficial and accessible to surgical approach. Because the pyramidal tract is difficult to reach and the corticospinal tract not well isolated in the spinal cord, these sites were considered unsatisfactory. In the cerebral peduncle it seemed that the corticospinal fibers might be sectioned with little danger of injury to other structures which might complicate the clinical result. Moreover, since it seemed likely that many extrapyramidal motor pathways might not be passing through the peduncle, there remained the possibility that some useful motor power might be retained or be recovered after the operation.

According to current textbooks, the basis pedunculi is composed from lateral to medial aspects of the following fibers tracts:

parieto- and temporo-pontine, cortico-spinal and fronto-pontine. The origins and function of the lateral bundles are not known. Section of the basis pedunculi in monkeys produces a contralateral hypotonic hemiparesis with increased tendon reflexes, but without alteration of the plantar reflex. This clinical picture differs from that produced by cortical ablation of the motor areas in that the hemiparesis is hypotonic, and from that resulting from pyramidal lesions in that it is associated with hyperreflexia (4).

Case Report: E. A. (#453744)—a 49-year old negress was admitted to The Johns Hopkins Hospital March 8, 1948 complaining of jerking movements of the right arm, leg and face for three weeks. One evening in February 1948 the right hand and foot suddenly began to wriggle. The involuntary movement could not be stopped even by holding the limb with the left hand. After 2-3 days the wriggling ceased. For several days the patient felt normal, but about 2 weeks before admission she noticed the movements again. At first they were slight, but within a day they had become so violent that the patient was unable to get out of bed. The right arm and leg were primarily involved but when the jerkings were at their acme, practically all of the muscles of the right side of the body took part in the movements. Any form of mental, emotional or physical exertion aggravated the wriggings and conversely mental and physical rest tended to decrease their severity. Only during sleep did the movements entirely disappear.

The patient's past, family and personal medical histories were otherwise irrelevant.

The patient, a well developed, middle aged negress, had constant grotesque movements of the right extremities and right side of the body. On general physical examination few abnormalities were noted. Although the patient's blood pressure was elevated (180/100) her heart was not enlarged and her heart sounds were normal.

The patient was well oriented, and cooperated well in a neurological examination. Except for irregular slow spasmodic movements of the right side of the face the cranial nerves appeared to be in order. All modalities of sensation were intact throughout the body. The tendon reflexes were active and approximately equal on the two sides of the body. Both plantar reflexes were flexor. To gross testing the muscular power was normal throughout. However, the coarse irregular movements of the right arm and leg made it difficult to examine the strength accurately. The coordination of the right extremities was markedly impaired because of the involuntary movements. Walking was impossible. No fibrillations were noted.

With the patient lying in bed the movements of the upper extremity consisted of serial abduction and adduction of the extended arm associated

with pronation and supination of the forearm and flexion and extension of the fingers. These movements recurred 1-3 times per second. When the wriggles were more severe the arm would be flung over the head, the forearm flexed, and then the arm abducted and finally adducted to the side. This movement might be repeated with variations once or twice a second.

Rotatory pelvic movements occasionally lifted the right flank from the bed. These gyrations were accompanied by contractions of the abdominal muscles.

The movements of the right leg consisted of abduction and adduction of the thigh associated with inversion and eversion of the foot occurring 2-3 times per second. Occasionally the leg was lifted off the bed and the knee flexed.

The facial grimaces, never very pronounced, seemed to accompany a slow elevation and depression of the right shoulder.

The routine urinary and hematological examinations did not bring out any abnormalities. The blood sugar was found to be 130 mg. percent and 100 mg. percent on two occasions. Roentgenograms of the skull and pneumoencephalograms were normal. Electroencephalograms, made after administration of sodium pentothal (*sodium* ethyl thiobarbiturate) on one occasion and intocostin (a curare preparation) on another occasion, were reported as having an amplitude asymmetry, the activity of the entire left side being of lower voltage than that of the right side. The spinal fluid was normal in all respects.

The patient was observed for a week. During this period the movements continued during the waking hours unabated. Within a minute after arousing from natural or artificially induced sleep (pentothal sodium) the movements would appear in the arm and leg, then gradually increase in severity and amplitude over a period of 1-2 minutes. They would continue at this level unless the patient was absolutely quiet and undisturbed when they became less pronounced, unless the patient was excited when the movements increased. Complete abolition of the movements only occurred during sleep. Hypnosis temporarily decreased the movements of the arm and abolished those of the leg.

On March 12, 1948 a pneumoencephalogram was made after the removal of 100 cc. of spinal fluid and its replacement by 100 cc. of air. The ventricular and subarachnoid systems appeared normal. The procedure was carried out under sodium pentothal anesthesia; immediately upon awakening from the anesthetic the movements returned and rapidly reached their former severity.

On March 16, 1948 a section was made of the left cerebral peduncle. A vertical incision was made in the right temporal region and carried down to the zygoma. The temporal muscle fibers were split and the squamous portion of the temporal bone was perforated. The opening was enlarged to approximately 5 cm. in diameter. An incision was then made in the dura mater allowing the temporal lobe to be lifted up. No vessels had to be coagulated. Gentle retraction of the temporal lobe brought the cerebral peduncle into view. The lateral sulcus of the mesencephalon was an ill defined groove. The 4th nerve and the superior cerebellar artery were identified. Eventually, the entire lateral half of the cerebral peduncle was visualized. In an avascular area an

incision approximately 6-7 mm. in depth was made into the peduncle from the lateral sulcus medially for a distance of approximately 2 cm. In all probability the medial quarter to one-third of the peduncle was left intact. There was no bleeding in this portion of the procedure. (Fig. 1). The temporal lobe was then allowed to fall back into place. The wound was closed in anatomic layers. The patient was in good condition throughout the entire procedure.

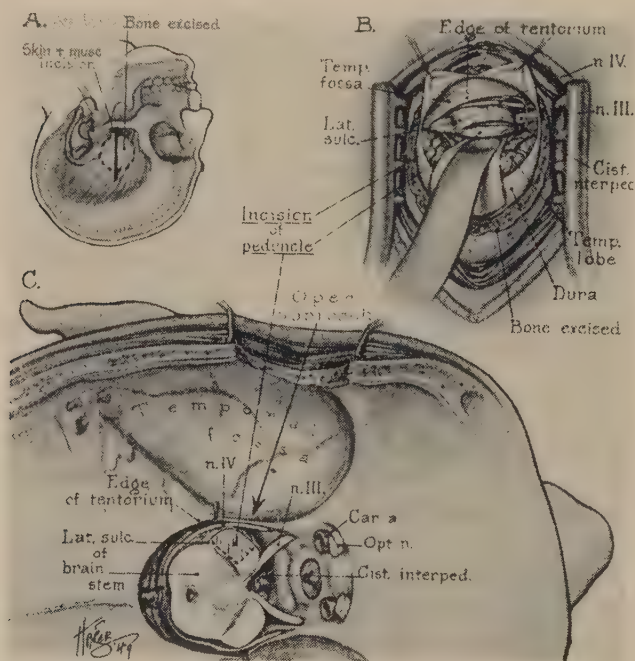


Fig. 1.

The operative approach for section of the cerebral peduncle is indicated. A. The head hangs down to allow the temporal lobe to fall away from the floor of the middle fossa. B. By gentle retraction the incisura tentorium is exposed and the arachnoid incised over the brainstem. The peduncle is well visualized, and the incision made from the lateral sulcus medially. C. A sketch to show the relations in the operative field.

Upon awakening from the anesthetic the patient was free of all involuntary movements but had a complete right hemiplegia. She responded by simple words to questions although she was not heard to formulate sentences.

On the morning of the first postoperative day the patient complained of difficulty in seeing, presumably due to the apparent internal strabismus of the left eye. Her speech was slurred but intelligible. She could move the fingers of her right hand feebly and her right leg fairly well.

On the second postoperative day a few feeble involuntary movements of the right shoulder were seen.

On March 21, 1948, the fifth postoperative day, the patient was up in a wheelchair. She still complained of diplopia, the images being side by side. Her right arm and leg were moved unsteadily with some effort, and after such an attempt a few involuntary jerks of the arms and shoulder muscles were noted for a few seconds. The right arm was flaccid at finger, wrist, elbow and shoulder.

The patient's visual acuity was good in each eye and her visual fields were grossly normal. The pupils were each 3 mm. in diameter and reacted well to direct light and in accommodation. There was a slight ptosis of the left eyelid. External ocular movements were full and without nystagmus. The corneal reflexes were active and equal.

The right hand could be feebly clenched, the wrist and elbow moved but the arm could not be lifted above the shoulder. All modalities of sensation appeared normal. The tendon reflexes were practically absent, only a flicker being present on the left side. No response could be obtained on plantar stimulation on either side.

Her condition continued to improve and she was discharged on March 26, 1948. At that time she was able to walk without assistance, but the right leg was dragged. Her speech was somewhat jerky but she could talk coherently. Her mentation was clear.

No abnormality could be found in her cranial nerves. The diplopia, previously noted, had gone.

At rest she had a few involuntary movements of the shoulder which could be controlled at will. The right arm was quite weak at all joints but could be elevated to shoulder level. The muscles of the right side of the trunk and right leg were weak but all movements were well performed. Both the right arm and leg were hypotonic. The tendon reflexes were absent on the right, sluggish on the left side.

The patient was readmitted to the hospital on May 24, 1948 in coma. She had been doing well at home until approximately two weeks before admission, when she began to have clouded, confused episodes lasting a few minutes. The night before admission she had a generalized convulsion and the morning of admission a second one, both beginning on the right side.

On examination the patient was deeply comatose, thrashing about wildly at times. Her blood pressure was 182/118. Her breath had a strong odor of acetone. The site of the cranial defect was flat. The right extremities appeared weaker than the left and the right reflexes hyperactive. The remainder of the neurological examination was negative.

Urinalysis on admission was reported as sugar 4/; acetone 4/, diacetic acid 4/, and the blood sugar was 532 mgm. percent. On diabetic treatment her coma rapidly cleared.

As the patient became coherent it was apparent that she had a mild aphasia which rapidly cleared. At no time did she have severe involuntary movements, although a few jerkings were seen at times in the right hand.

The patient was seen again on April 14, 1949. She stated that she had only minimal jerks of the right hand at rest, although if she became excited the movements were more pronounced. She had been doing all her own housework without difficulty. Her only complaint was that she occasionally had a catch in the right hip when walking. She was following her diabetic diet and taking insulin.

On inquiry she stated that the first three fingers of the right hand ached and felt numb although she never dropped objects from her hand. Her memory had improved from its preoperative state.

She appeared to be in excellent general health. No evidence of aphasia was apparent. The cranial nerves were all functioning normally. The strength of the right arm was generally reduced and the right grip was less than the left (average of 3 dynamometer readings, 55 right, 65 left). There was little difference in the resistance to passive manipulation of the arms. Perhaps the right was slightly hypotonic as compared to the left. The strength of the legs appeared equal and adequate and the muscular tone normal. The tendon reflexes were slightly hyperactive on the right side but the plantar reflexes were flexor. Coordination tests were well performed, even fine movements of the fingers being carried out dextrously. All modalities of sensation appeared to be normal. The patient walked on a normal base steadily.

If the right hand were observed for several minutes a few slow irregular movements of the fingers could be seen at intervals. There were no apparent movements of the right arm or leg.

DISCUSSION

On the basis of one case without histological control, only a few generalized conclusions are warranted. In the first place it seems apparent that partial section of the cerebral peduncle may be accomplished without incapacitating neurological sequelae. Whether in this case the remarkable recovery of motor function is due to the presence of uncut fibers in the peduncle or to extra-peduncular fibers cannot be answered definitely at this time. However, further experience has indicated that the paralysis may be much more severe if a more extensive section is made of the peduncle. The genesis of the mild hypotonicity can only be speculated upon; complete peduncle section may be associated with spasticity. It seems certain that section of the cerebral

peduncle will effectively abolish the abnormal movements of hemiballismus, and as other experiences have shown, of Parkinson's disease (10). This is not unexpected in view of the current theories of the physiological basis of tremor.

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Les Hématomes sous-duraux Calcifiés

Par

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Les hématomes sous-duraux chroniques figurent actuellement dans la pathologie neurochirurgicale une lésion bien définie, prévue par la clinique, familière à l'opérateur. Les temps présents ne se soucient plus de les différencier d'avec les hémorragies spontanées de la pachyméningite hémorragique, tout au plus prennent-ils encore intérêt, reconnaissant à leurs origines la qualité traumatique, aux mécanismes de leur enkystement, à leur évolution, aux modalités techniques de l'intervention. Depuis le mémoire de *Putnam* et *Cushing*, les observations se sont multipliées. Mais de cette actuelle banalité il est permis d'extraire certains faits qui méritent d'être appréciés en eux-mêmes parce qu'ils échappent aux descriptions désormais classiques et consacrent l'individualité d'une forme clinique particulière.

L'observation que nous rapportons prétend à ces mérites.

Observation (Obs. 1325). R. . . . Félix, est un sous-officier de 29 ans. Il fut hospitalisé pour la première fois le 14 Mars 1944 dans le service de neuro-psychiâtrie de l'Hôpital Militaire Desgenettes (Médecin-Leutenant Colonel *Hamon*) pour des « troubles parétiques transitoires du membre supérieur droit et de l'hémiface droite. »

Rien de particulier n'est à signaler dans ses antécédents héréditaires et collatéraux.

Dans ses antécédents personnels, on relève : absence de maladies graves dans l'enfance ; aurait commencé à marcher assez tard ; à 5 ans, chute sur la tête provoquant une plaie contuse de la région frontale gauche (pas de perte de connaissance) dont il subsiste une cicatrice cutanée assez importante. Scolarité normale jusqu'à 13 ans ; est employé comme apprenti mécanicien jusqu'à 18 ans, âge auquel il entre dans l'armée.

L'histoire de l'affection pour laquelle il est hospitalisé est la suivante : il y a 18 mois environ, alors qu'il était occupé à travailler sous une voiture, il voit s'installer une impotence de la main et du membre supérieur droit, avec dysesthésies (fourmillements) au niveau des doigts et du bord cubital de la main et de l'avant-bras. Seuls les fourmillements gagnent l'hémiface droite, avec sensation d'anesthésie et gêne légère de la parole. Pas de phénomènes convulsifs. Le tout disparaît sans séquelles, en 10 minutes environ, d'après le

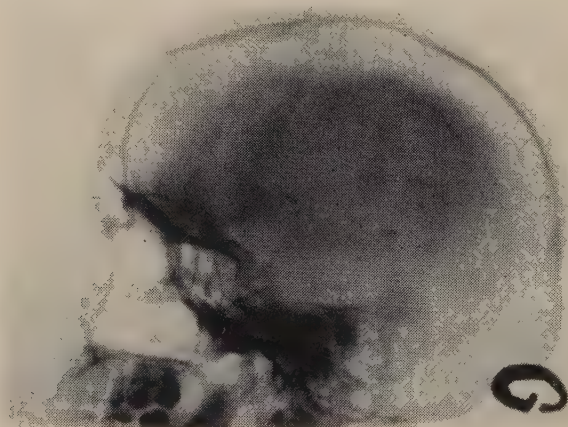


Fig. 1.

Radiographie de profil.

malade. Le deuxième incident a lieu il y a 10 mois, identique au précédent. Les doigts se mettent en griffe et l'avant-bras en flexion, puis tout rentre dans l'ordre. Il y a 4 mois, troisième incident semblable, de plus courte durée (5 minutes), sans séquelles. Entre les crises, le malade accuse des céphalées sus-orbitaires gauches intermittentes. Il n'y a pas de signes pouvant faire penser à un syndrome d'hypertension intracrânienne.

A l'examen, on se trouve en présence d'un sujet normalement musclé, n'ayant pas maigri et ayant un bon état général. La marche et la station debout sont normales. Il n'y a pas de signe de Romberg. Au point de vue neurologique, on ne peut retenir qu'une hyperextensibilité des membres droits, sans signes d'irritation pyramidale, ni syndrome déficitaire. L'examen oculaire ne montre absolument aucune anomalie, tant en ce qui concerne les musculatures intrinsèque et extrinsèque, que le fond d'oeil, la tension rétinienne, le champ visuel et l'acuité visuelle (V.O.D.G. : 10/10).

Le reste de l'examen somatique est entièrement normal. La tension artérielle est à 9,5/7 au Vaquez. Une réaction de B.W. pratiquée dans le sang le 29 Mars s'est révélée négative.

Le libellé de l'examen radiologique du crâne fait à cette date est le suivant : vaste image ovoïde de 10 cms de long sur 6 cms de large, à grand axe antero-

postérieur intéressant la région fronto-parietale gauche ; l'aire manque d'homogénéité ; la raréfaction osseuse prédomine créant un contour circiné clair particulièrement visible aux limites antérieures de l'image. De petites calcifications se surajoutent, comme au hasard ; la stéréoradiographie les situe près de la table interne. Cet examen fait penser à un méningiome (Fig. I et II).

Le malade sort de l'hôpital le 29 Avril 1944 et reprend son service jusqu'au 19 Juillet, date à laquelle il est de nouveau hospitalisé. On ne note aucune

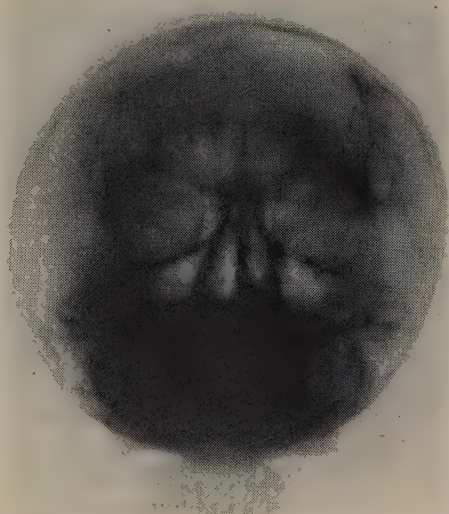


Fig. 2.

Radiographie de face.

symptomatologie fonctionnelle, l'examen neurologique est normal et l'état général toujours très bon.

Une nouvelle radiographie crânienne montre une image sans changement depuis le précédent examen et la radiologie conclut « la saillie interne ovoïde, pariéto-frontale, parsemée de taches calcifiées, peut répondre à un méningiome ou à un hématome calcifié ».

L'examen ophtalmologique est sans changement.

Le malade, qui n'est pas décidé à se faire opérer, reprend son service le 25 Juillet 1944 et l'assure régulièrement jusqu'au 11 Avril 1946. Il est alors hospitalisé à Clermont-Ferrand parce qu'il présente depuis trois semaines des « douleurs continues et sourdes de la région temporale gauche ». Le 14 Mai, il est évacué sur l'Hôpital Militaire Desgenettes. En dehors des céphalées temporo-pariétales gauches et d'une diminution de la force segmentaire de l'avant-bras droit, l'examen des fonctions motrices, sensorielles, réflexes et sensitives est entièrement négatif.

Une nouvelle radiographie crânienne est pratiquée. En voici le compte-

rendu : L'examen actuel (12 Mai 1946) montre la parfaite stabilité radiologique de l'image endocranienne dont l'aspect ne s'est pas modifié, ni dans ses dimensions, ni dans sa tonalité, depuis l'examen du 8 Février 1944. Des planigrammes ont été pratiqués de $\frac{1}{2}$ cm en $\frac{1}{2}$ cm à partir de 0,5 cm du plan d'appui temporo-pariétal gauche. Les coupes les plus superficielles montrent qu'il existe, près de la table interne et du diploé, une éburnéation irrégulièrement répartie ; cette éburnéation se reconnaît à l'existence de

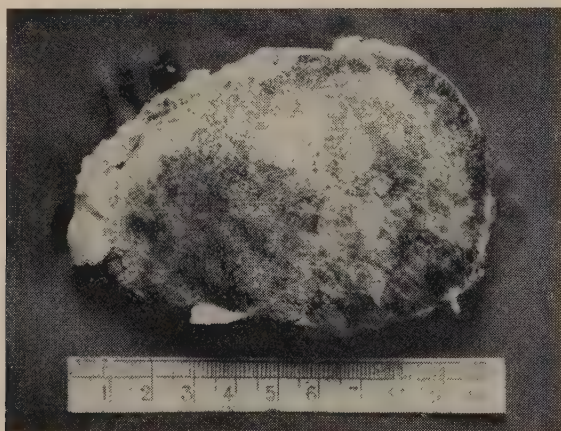


Fig. 3.

Pièce opératoire face.

petites plaquettes claires disséminées, qui tendent à s'agminer au voisinage de la suture fronto-pariétale. La zone tumorale elle-même est cernée par un sillon discontenu que soulignent les calcifications les plus périphériques. Dans le sens de la profondeur, la néoformation (dont on peut suivre le développement grâce aux inclusions calcaires) paraît s'étendre jusqu'à 3 cms du plan d'appui cranien.

Le diagnostic est toujours incertain : S'agit-il d'une tumeur endocranienne superficielle type psammome ou d'un méningiome calcifié, ou plus simplement d'un hématome secondairement organisé ?

Le 13 Mai 1946, le malade est évacué sur le service de neurochirurgie de l'hôpital Edouard Herriot : l'examen neurologique est toujours entièrement négatif.

Le 17 Juin, vers 21 heures 30, apparition de petits troubles parétiques du membre supérieur droit dont la durée est de 5 minutes environ ; violents céphalées fronto-pariétales concomitantes, pas de nausées.

Le 20 Juin, le B.W. dans le sang est négatif.

Le 24 Juin, la radiographie (Dr. Levy) montre l'existence d'une petite plaque vasculaire calcifiée pariéto-frontale gauche moyenne avec quelques doubles contours bien nets. Donc tumeur méningée vasculaire calcifiée en plaques.

Le 1 Juillet (Pr. *Dechaume*) : Ce militaire de 28 ans présente depuis quelques années des crises jacksonniennes au niveau du membre supérieur droit, suivies de parésie transitoire intéressant surtout le bras, les crises n'ayant intéressé que ces derniers temps la jambe. L'examen neurologique étant entièrement négatif, il faut retenir dans son histoire une chute à l'âge de 5 ans, avec plai contuse dont on retrouve une cicatrice dans la région frontale gauche.

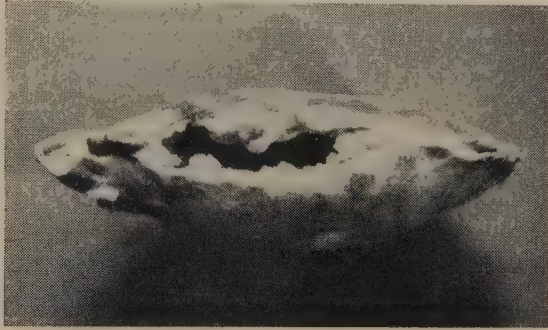


Fig. 4.

Pièce opératoire profil.

Alors que tous les examens viscéral, cardio-vasculaire, neurologique et ophtalmologique sont négatifs, la radiographie seule nous montre l'existence de calcifications dans la région frontale et pariétale gauche. On a l'impression qu'à la partie antérieure de la zone calcifiée, il existe des lésions osseuses avec une vascularité anormale de l'os. Les calcifications semblent tapisser les parois d'une poche ovoïde aplatie de la région fronto-pariétale gauche.

Les lésions osseuses seraient en faveur d'un méningiome à évolution extrêmement lente, mais on peut, étant donnée la forme de cette tumeur ovoïde, se demander s'il ne s'agit pas d'un kyste hémattique contemporain du traumatisme survenu à l'âge de 5 ans, dont les parois seraient calcifiées et qui, ayant subi une organisation conjonctivovasculaire, a entraîné des modifications de la vascularisation osseuse. L'indication opératoire est formelle, en prévenant le chirurgien que les modifications osseuses vasculaires sont surtout à la partie antérieure de la lésion. On fera un large volet, débordant en avant, en haut et en arrière, les limites des calcifications.

Le 2 Juillet, intervention (Pr. *Wertheimer* — Dr. *Mansuy* — *Sermonnard*) — Large volet fronto-pariétal gauche. Vascularisation anormale de l'os à la partie antérieure. La dure-mère adhère légèrement au squelette. Il existe, correspondant à toute la zone découverte, une plaque osseuse située sous la dure-mère, lui adhérent de façon serrée, sauf en avant, où il existe une petite poche de liquide clair. En libérant le lambeau dural de cette plaque osseuse, on ouvre une cavité renfermant une masse blanc-jaunâtre rappelant le sébum,

quoique de teint plus jaune. On se rend compte que la néoformation a une topographie strictement analogue à un hématome sous-dural chronique, la paroi superficielle étant représentée par la lame osseuse, le contenu étant constitué par ce sébum, la paroi profonde, non ossifiée, n'adhérant pas au cortex qu'elle n'envahit pas, mais recevant de lui une importante vascularisa-

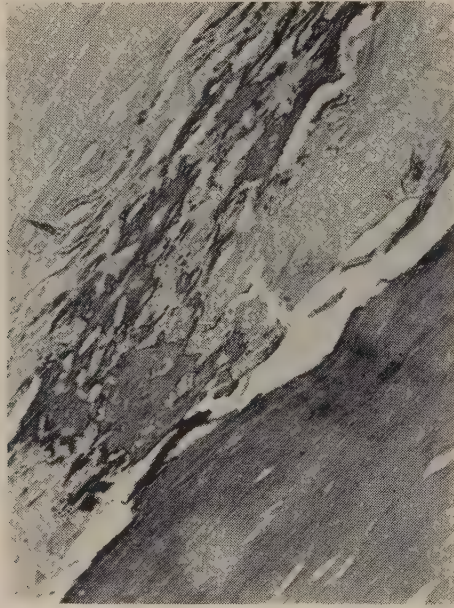


Fig. 5.

Calcifications de la paroi.

tion. Ablation de la poche presque en totalité, quelques petits fragments osseux étant laissés sur les bords et enlevés après coup. Hémostase, suture et suspension de la dure-mère. Injection de cent mille unités de pénicilline dans la cavité et fermeture sur un drain.

Il s'agit vraisemblablement d'un ancien kyste traumatique sous-dural à parois surchargées de sels calcaires.

Suites opératoires : Après l'intervention, apparition d'une monoplégie supérieure droite, accompagnée de gros troubles de la sensibilité profonde, qui dure 15 jours. Puis le malade se sent bien et à sa sortie de l'hôpital, le 29 Juillet il semble complètement rétabli.

Le 13 Octobre 1947, plus d'un an après l'intervention, le malade convoqué par nos soins, a déclaré avoir eu, depuis son intervention 5 crises comitiales généralisées avec début par le membre supérieur droit et extension rapide à tout le côté droit, puis perte de connaissance avec morsure de la langue et miction involontaire. Ces crises, d'une durée de 5 minutes, sont complètement

amnésiques et se terminent par une céphalée d'une heure environ. Le malade a repris ses occupations, car entre ses crises il n'a que de très rares céphalées et quelques crispations de la main droite durant quelques minutes. Ces crises, au dire du malade, sont presque toujours survenues à l'occasion d'un écart de régime.

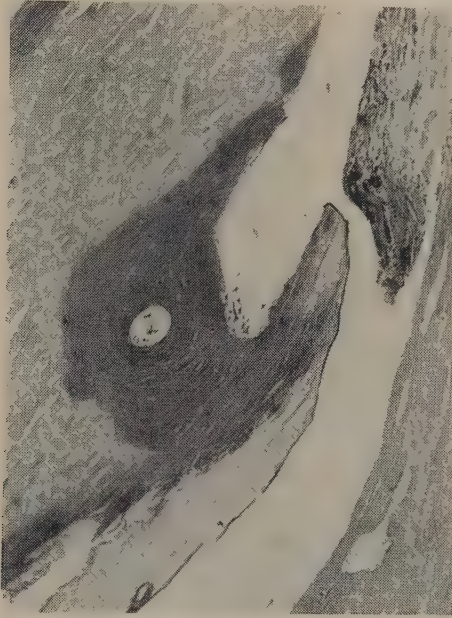


Fig. 6.

Ossification dans la paroi.

L'examen neurologique est entièrement normal, on ne trouve pas de syndrome déficitaire. Signalons que malgré les prescriptions qui lui ont été faites, le malade ne prend pas de gardénal.

Des observations de ce type ont été rapportées, mais en petit nombre. Il en est fait mention par *Lewis* (1889) comme d'une découverte exceptionnelle à l'autopsie d'aliénés, *Elsner* (1896) décrit les calcifications de la pachyméningite hémorragique, *O'Sullivan* (1925) cite l'hématome calcifié parmi les calcifications intracrâniennes. Mais les premières descriptions sont dues à *Goldham* et *Critchley*; *Schuller* en 1935 en publie 4 cas dont les compte-rendus sont purement radiologiques. *Dyke* et *Davidoff* rapportent deux observations dans lesquelles l'hématome calcifié apparaît comme la séquelle d'un traumatisme obstétrical;

Munro, un cas d'hématome sous-dural calcifié consécutif à un traumatisme crânien vieux de douze ans ; *Clovis Vincent* (1934) cite l'observation d'un homme de 42 ans, traumatisé 9 ans auparavant. Signalons encore les faits publiés par *Samson, Caron* et

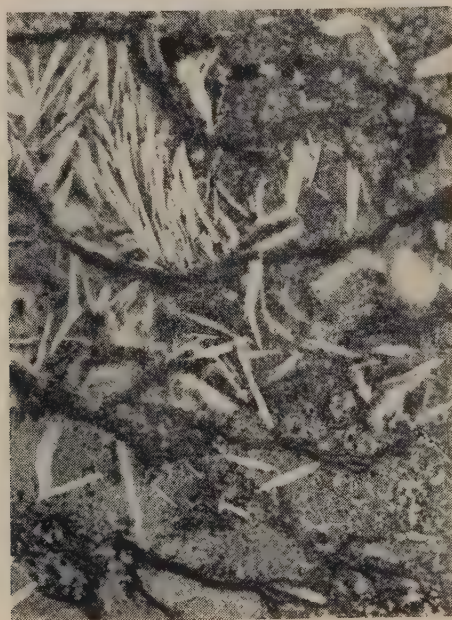


Fig. 7.

Cristaux de cholestérine.

Desrochers et par *E. Lang* en 1943. L'unique mémoire consacré à ce sujet est celui de *D. A. Boyd* et *P. Merrel* tirant prétexte d'un cas recueilli par ces auteurs. Une monographie récente consacrée par *Asenjo* aux hématomes sous-duraux chroniques (1947) fait mention de l'hématome calcifié et d'une observation personnelle.

CONSIDERATIONS CLINIQUES

A vrai dire elles se distinguent à peine de celles par lesquelles fut individualisé l'hématome sous-dural chronique. La calcification de l'hématome n'ajoute rien aux caractères de cette longue période d'intervalle libre et de latence qui s'interpose entre le

traumatisme initial, qu'il soit patent ou très discret, et la période où se manifestent les signes d'hypertension intracrânienne ou d'irritation corticale. Vainement chercherait-on dans l'analyse séméiologique des signes qui lui soient propres. Mais les manifestations hypertensives ou les crises épileptiques, qu'elles revêtent ou non un caractère bravaï-jacksonien, imposent la radiographie crânienne qui seule est révélatrice de l'hématome sous-dural calcifié. Il est exceptionnel en effet que la simple radiographie mette en évidence un hématome sous-dural chronique, hormis le cas d'une déformation de la voûte dont nous avons recueilli un exemple récent. L'encéphalographie en l'absence d'œdème papillaire, et de préférence la ventriculographie, sont nécessaires à l'affirmation du diagnostic. Au contraire, les clichés osseux, dans le cas d'un hématome calcifié, sont riches d'enseignements. Il est possible, à l'aide des documents publiés, d'en décrire les éléments essentiels. Le squelette de la voûte apparaît parfois anormalement vascularisé, mais surtout les calcifications dessinent comme la paroi d'une poche kystique. Sur les profils qui correspondent aux faces de l'hématome, on aperçoit un double contour calcifié, renforcé par endroits de zones plus sombres. À l'intérieur de cette ligne sont disposés irrégulièrement quelques calcifications. Sur les clichés de face qui montrent l'hématome en coupe, le double contour se retrouve avec des zones plus denses disposées aux deux pôles.

Sur ces bases, le diagnostic se trouve simplifié ; la radiographie est suffisamment démonstrative. Encore convient-il d'éliminer les causes d'erreur auxquelles peut prêter la vision de calcifications intracrâniennes. Nous ne nous attarderons pas à celles de la sclérose tubéreuse de *Bourneville*, ombres isolées et profondes ; aux traînées fluxueuses, entrelacées, vermiculaires, d'aspect festonné de l'angiomatose calcifiée des méninges, dite plus justement maladie de *Knud Krabbe*, aux images calcifiées des kystes hydatiques visibles en plein parenchyme cérébral, à celles superficielles mais petites et nodulaires de la cysticercose méningée, aux calcifications basales des craniopharyngiomes.

Par contre, certains méningiomes, les tuberculomes parfois, des gliomes à évolution lente peuvent prêter à confusion. En vérité les méningiomes corticaux s'accompagnent le plus souvent d'altérations osseuses de la voûte : images en palissade, hyperostoses ; l'ombre d'un tubercule calcifié est unique, souvent arrondie, de contours irrégulier les calcifications de certains astrocytomes ou oligodendrogliomes sont le fait de calcosphérites histologiques dont la confluence dessine des ombres plus ou moins denses, inégalement réparties. Tous ces aspects sont bien différents des calcifications denses de l'hématome sous-dural, et plus éloignés encore de la coque calcifiée découverte chez notre malade avec son double contour épousant en dehors le dessin de la voûte et en dedans par sa concavité la corticalité de l'hémisphère.

CONSIDÉRATIONS ANATOMOPATHOLOGIQUES

L'hématome sous-dural chronique calcifié n'a pas plus d'individualité anatomique que clinique. Il se développe dans l'espace sous-dural actuellement bien défini ; il est le fait d'hémorragie en provenance des vaisseaux perforants, anastomoses jetées à travers l'espace sous-dural entre la circulation méningée et la circulation corticale, ou des granulations de Paccioni. L'opérateur isole facilement la duremère qui se clive de la paroi externe de l'hématome ; il peut également séparer la paroi interne de la méninge molle et procéder à l'extraction de la tumeur sans ouvrir les espaces arachnoïdiens. Dans le cas que nous rapportons, l'exérèse fut pratiquée selon ces principes, mais l'ouverture de la poche en cours d'intervention donna issue à une substance rappelant un peu le contenu d'un kyste dermoïde.

La pièce apparaît comme une tumeur dure, irrégulière et ovalaire avec deux faces convexes rappelant un peu l'aspect d'une huitre, et deux pôles amincis (fig. 3 et 4). Les parois en sont dures, osseuses, surtout la paroi externe. Le contenu représente une sorte de bouillie brunâtre.

Des examens histologiques ont permis de préciser la structure pariétale. La paroi conjonctive est constituée par de larges trousseaux fibreux collagènes, avec peu de noyaux cellulaires et une vascularisation réduite. Sur de larges étendues, ces trousseaux collagènes ont une coloration noirâtre imputable à des imprégnations calciques rappelant celles qu'on observe dans certaines artères athéromateuses (fig. 5). Mais, outre les calcifications, les coupes montrent des points d'ossification histologique avec l'image d'un canal de Havers typique (fig. 6).

Quant au contenu de la tumeur, il est constitué par des vestiges de polynucléaires et de macrophages sur un fond granuleux, par des cristaux de cholestérine (fig. 7) et par des cadavres cellulaires enfermant des calcifications histologiques.

La structure est donc typiquement celle d'un hématome sous-dural chronique ; elle est conjonctivovasculaire et fibroconjonctive. Les calcifications sont le fait d'une surcharge calcique pariétale et de la dégénérescence cholestérinienne de certains éléments dans la masse nécrotique centrale. Mais la constatation d'un point d'ossification mérite d'être retenue. En vérité cette osteogénèse localisée n'intervient que de façon tout à fait accessoire dans l'image radiologique. En outre une seule coupe a révélé l'image d'une formation osseuse individualisée.

La pathogénie de l'hématome sous-dural chronique calcifié n'implique aucune considération particulière. L'organisation de l'hématome dont nous avons indiqué les origines, sa transformation en caillot sont le fait des battements cérébraux ; son cloisonnement est réalisé grâce à la constitution d'un tissu conjonctif lâche à la périphérie ; son accroissement est imputable à des hémorragies secondaires. La fibrine se transforme en collagène et les cellules conjonctives en fibroblastes. La seule particularité sur le plan anatomique comme sur le plan clinique tient aux calcifications. Les unes affectent le contenu de la tumeur ; il s'agit de précipitations qui s'opèrent au voisinage de cellules mortes qui sont sans doute des vestiges de macrophages ; il s'agit là d'un processus banal. Plus remarquables sont les dépôts calcaires qui

s'effectuent dans la paroi et s'intriquent dans des trousseaux fibreux très denses ; ils rappellent ceux que *Leriche* et *Policard* ont décrit dans les vaisseaux athéromateux et dans les parois des anévrysmes. Quant à la découverte de plages osseuses, elle pose le problème de l'ostéogénèse locale et de l'ossification hétérotopique. L'hématome sous-dural, milieu ossifiable, chargé de tissu conjonctif jeune, constitue pour l'ossification metatraumatique un milieu idéal propre à satisfaire les conceptions exposées par *Leriche*. Dans ce cas particulier l'ostéogénèse était réduite à une figuration histologique et très limitée.

CONSIDERATIONS THERAPEUTIQUES

Elles seront brèves et formelles. La découverte radiologique d'un hématome calcifié impose l'exérèse chirurgicale en masse de la tumeur. Si l'hématome sous-dural chronique habituel peut en certaines circonstances s'accomoder de la simple évacuation de son contenu par une trépanation limitée, l'hématome calcifié exige d'être enlevé en totalité par un large volet. Le geste est simple ; il n'exige dans son exécution qu'une hémostase rigoureuse à l'insuffisance de laquelle peut pallier dans une certaine mesure un petit drain sous-dural, précocement retiré.

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